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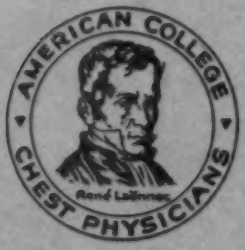
VOLUME XIX NUMBER 4

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



PUBLISHED MONTHLY

APRIL
1951

EXECUTIVE OFFICE, 500 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS
PUBLICATION OFFICE, ALAMOGORDO ROAD, EL PASO, TEXAS

Entered as Second Class Matter August 18, 1930, at the Postoffice at El Paso, Texas
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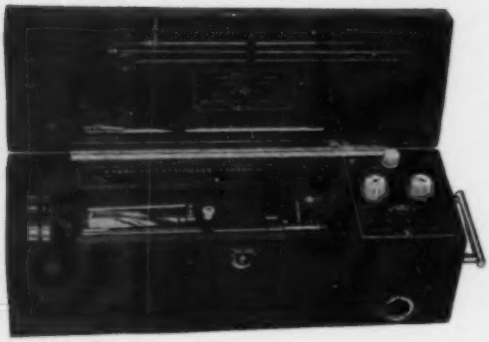
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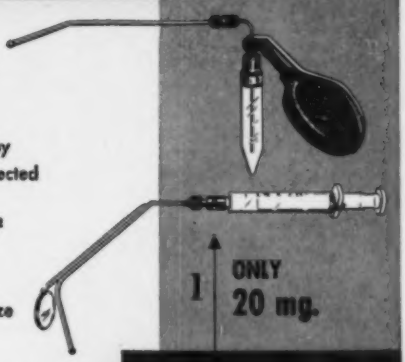
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1. Carabelli, A.: *Diseases of the Chest*, 15:332, May, 1949 (167 cases; balance to be published).
2. Available from George P. Pilling & Sons, Co., 3401 Walnut Street, Philadelphia 4, Pa.
3. Miller, J. B., Mann, P., and Abramson, H. A.: *Diseases of the Chest*, 16:408, Oct., 1949.

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1. Krasno, L., and Rhoads, P. (1949), The Inhalation of Penicillin Dust: Its Proper Role in the Management of Respiratory Infections, Amer. Prac., 11:649, July.



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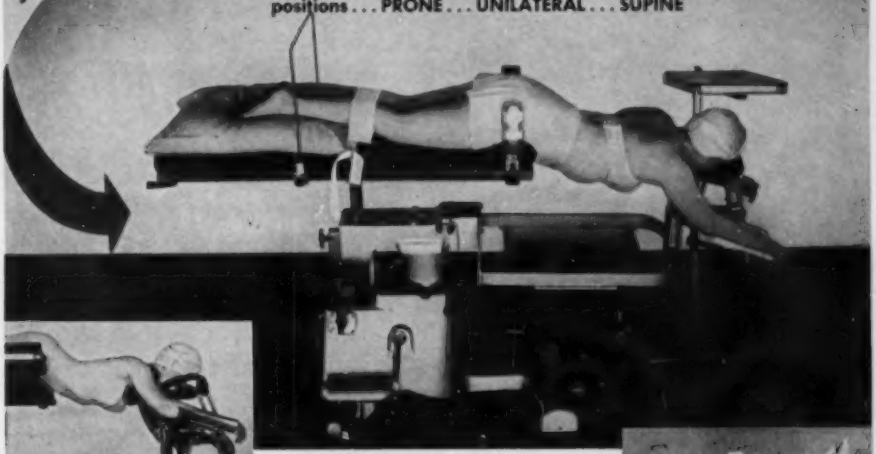
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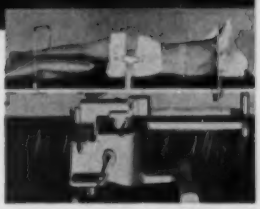
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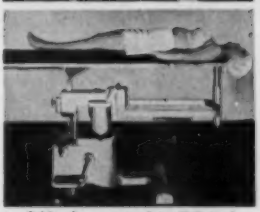


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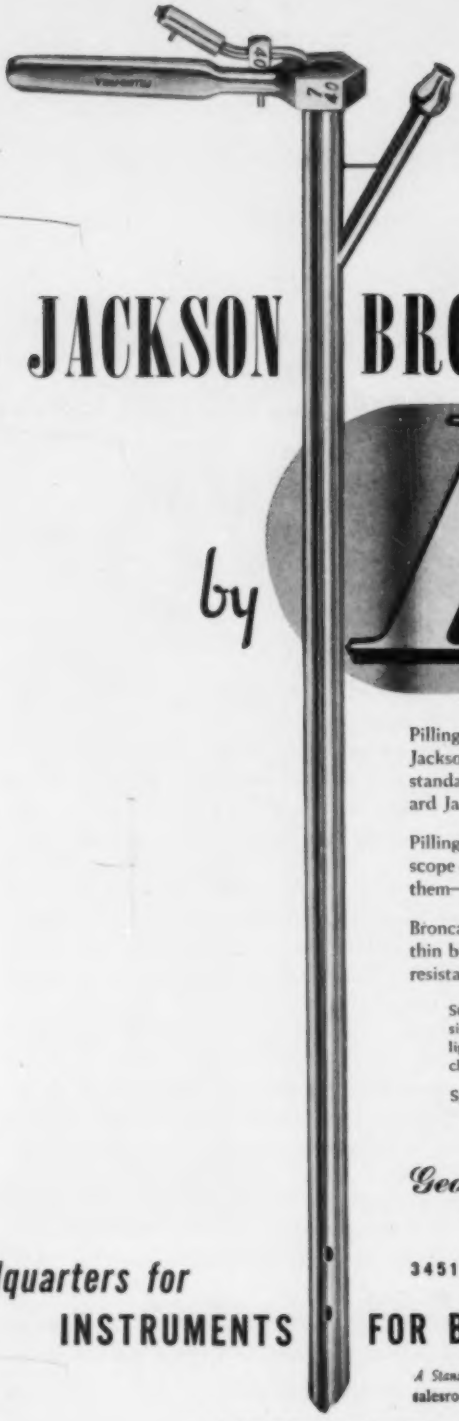
REFERENCES

1. Prigal, S. J.: Bacteriologic and Epidemiologic Approach to the Treatment of Respiratory Infections with Aerosols of Specific Antibiotics, Bull. N. Y. Acad. Med. 26:282 (Apr.) 1951.

2. Stovin, J. S.: The Use of Bacitracin in the Treatment of Sinusitis and Related Upper Respiratory Infections, New York Physician 32:14 (July) 1949.

3. Prigal, S. J., and Furman, M. L.: The Use of Bacitracin, a New Antibiotic in Aerosol Form; Preliminary Observations, Ann. Allergy 7:662 (Sept.-Oct.) 1949.

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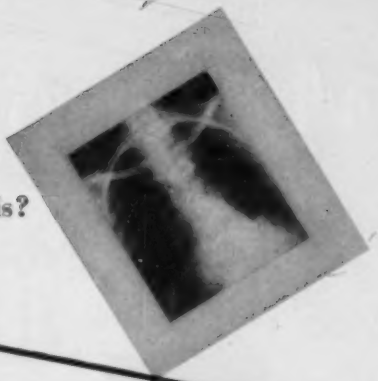
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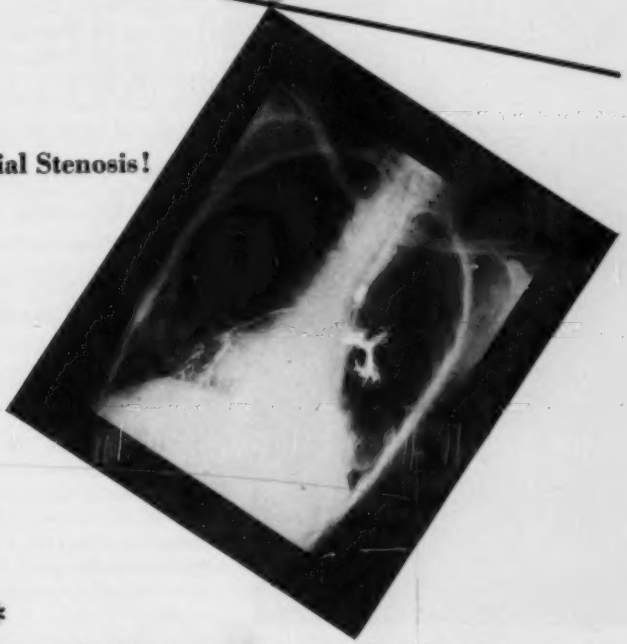
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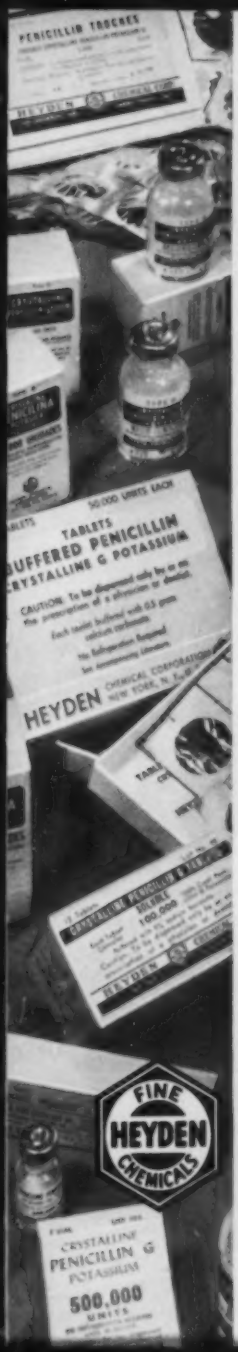
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DISEASES *of the* CHEST

VOLUME XIX APRIL 1951 NUMBER 4

The Combined Effect of Potassium Iodide and Streptomycin on Far Advanced Chronic Pulmonary Tuberculosis*

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Introduction

In this age of antibiotics and chemotherapeutic agents, far advanced chronic pulmonary tuberculosis stands almost alone among the bacterial diseases in its resistance to effective treatment by these agents. Since the isolation and extraction of streptomycin by Waksman in 1944, a large volume of experience in the treatment of all forms of tuberculosis has been accumulated. The cooperative study by the Veterans Administration is probably the most extensive of these investigations. With the accumulated experience of thousands of cases, one of the most consistent observations has been the almost complete refractoriness of patients having chronic pulmonary tuberculosis with cavitation. On the other hand, early exudative cases have been observed to exhibit dramatic improvement under streptomycin therapy. In the light of this experience, it seemed reasonable that any agent which might be active in mobilizing or changing in some degree the tissue barriers which are known to exist in chronic fibrocaseous tuberculosis, might well be advantageous in altering the natural history of the disease. In this manner the isolated organisms might be rendered more vulnerable to the action of some agent known to be active in vitro.

*All streptomycin was supplied by Merck and Company, Inc.
This investigation was supported (in part) by a research grant from the National Institutes of Health, Public Health Service.
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It is a well known clinical observation that gummata resolve and disappear rapidly under treatment with potassium iodide alone. In another granulomatous disease, tuberculosis, it has been repeatedly observed that iodides cause tubercle bacilli, previously absent, to appear in the sputum of infected patients. Jobling and Peterson in 1914 reported that iodine will combine with the unsaturated fatty acids obtained from tubercle bacilli and will neutralize their enzyme inhibiting properties. Subsequent to this neutralization, proteolytic enzyme action ensues within areas of caseation with liberation of the bacilli and their appearance in the sputum. They also stated that iodine might serve another purpose by facilitating solution and absorption of caseous matter, thus exposing the bacilli, which otherwise might be inaccessible to the influence of an effective therapeutic agent. In the light of this significant work, and in view of the relatively poor results obtained in the treatment of fibrocaseous tuberculosis with streptomycin alone, it seemed desirable to test the combined effect of potassium iodide and streptomycin against established tuberculosis in guinea pigs. These animal experiments were carried out in our laboratory with favorable results and have been reported previously.

Methods

Following these preliminary tests it was important to assay the combined effect of these two agents in patients having far advanced pulmonary tuberculosis with long standing cavitation, and in whom streptomycin alone would not be expected to offer any significant improvement. It was our purpose primarily to observe any significant changes which might appear on the chest x-ray film, with special attention paid to aggregate cavity diameters, as this affords a reasonably consistent quantitative method of estimation. It was also planned to carry out frequent sputum examinations and to determine the streptomycin sensitivity of the tubercle bacilli so obtained. Temperature, pulse, and respiration records were considered essential, as well as weekly weight determinations. Blood counts, sedimentation rates, blood chemical determinations and urinalyses were also necessary at frequent intervals for a comprehensive survey of the cases.

A total of 58 patients were selected for treatment at the Davidson County Tuberculosis Sanitarium and at the Vanderbilt University Hospital. In the majority of these we were able to confirm the presence of cavitation by chest x-ray films over periods of one to three years prior to study. None of the patients selected had received streptomycin previously and all were sputum positive at the beginning of treatment. The cases were divided into two

groups; 23 patients receiving streptomycin alone for a period of 120 days and 35 the combined treatment of streptomycin and potassium iodide over a similar period. Streptomycin was administered intramuscularly in a single injection of 1 gram daily to each member of both groups. Patients in the combined therapy group received, in addition, a total of 4 grams of potassium iodide daily by mouth, administered in three equal doses morning, noon and night. The saturated solution of potassium iodide diluted in 200 cc. of water was found to be the most satisfactory method of administration. All patients were restricted to complete bed rest, and received a high protein, high carbohydrate diet. They were weighed weekly. Bi-weekly sputum examinations were carried out, as were monthly streptomycin sensitivity tests. Both primary isolation and streptomycin sensitivity estimations were carried out on the classic egg yolk and agar solid media. Temperature, pulse, and respirations were recorded four times daily. Using these data, weekly averages were computed, in an effort to determine any large overall trends from week to week. Complete blood counts, sedimentation rates; urinalyses; blood chemical estimations of NPN, cholesterol, total serum proteins and the albumin-globulin ratio were performed every two weeks. Antero-posterior chest x-ray films were obtained on each patient immediately before treatment was instituted, and every two weeks thereafter during the 120 day period of observation. Before therapy was begun, all x-ray films were closely examined and measurements were made of all visible cavities. The cavity diameters were computed by calculating the average of the maximum and minimum diameters of a given cavity. In most instances each x-ray film revealed multiple cavities, in which case the aggregate cavity diameter was obtained from the sum of all the individual cavity measurements expressed in centimeters. This procedure was repeated after 120 days of treatment. In addition to measurement of cavities, an estimate was made of the approximate percentage of increase or decrease of exudate between the first and final films. This method of estimation of exudate is admittedly gross and subject to considerable error, but we believe it worthwhile, if only to reveal a trend in one or another direction.

Results

Temperature, Pulse and Respirations: By combining the weekly individual averages for temperature, pulse, and respirations, and obtaining a weekly average value for each of the two groups, no evidence was found of any significant difference between the controls, and the group receiving combined therapy.

Blood Counts: Most of the cases began the study with normal

white blood counts, and because of this no significant change could be observed. All of the patients having initial white blood cell elevations ended the treatment period with normal counts, but no significant difference could be observed between the two groups.

Red blood cell counts averaged between 3.5 and 4 million in both groups, and no apparent departure from this was noted in either group during this time.

CHART I

Cavity Measurements in Streptomycin Group

PATIENT	Aggregate Cavity Diameters in Centimeters		Net Change in Diameter During Treatment
	Before Treatment	After Treatment	
C.H.E.	5.3	3.7	−1.6
S.T.I.	6.5	6.5	0
W.I.L.	12.5	16.0	+3.5
M.C.K.	6.5	5.8	− .7
N.A.P.	0.6	2.2	+1.6
C.A.R.	3.1	3.0	−0.1
S.A.T.	2.0	2.5	+0.5
O.T.Y.	7.8	7.6	−0.2
V.A.U.	12.0	5.5	−6.5
E.L.T.	2.1	2.2	+0.1
M.A.S.	2.5	1.7	−0.8
R.E.T.	7.0	8.0	+1.0
W.O.D.	6.7	4.5	−2.2
B.U.R.	12.0	12.0	0
H.U.D.	2.2	2.2	0
S.W.T.	6.1	2.4	−3.7
W.E.N.	9.1	8.5	−0.6
F.R.H.	7.9	5.5	−2.4
G.I.D.	3.7	1.8	−1.9
P.E.S.	8.5	8.5	0
B.O.U.	7.0	6.0	−1.0
C.R.M.	6.0	6.0	0
F.K.I.	5.8	5.3	−0.5
TOTAL	142.9	127.4	−15.5
AVERAGE	6.2	5.5	− 0.7

The differential white counts remained within essentially normal limits for both groups. A few cases in each group showed a marked rise in eosinophils, but this finding was by no means consistent.

Sedimentation rates for both groups showed a moderate decrease during the period of treatment, but little if any relation could be established between clinical and radiographic improvement, and the behavior of the sedimentation rate.

Blood Chemical Determinations: Blood chemical determinations of NPN and cholesterol revealed no changes worthy of note. As was expected, an improvement in the general nutritional rate was reflected in an increase in total serum proteins.

Sputum: Out of 23 patients in the control group, four ended the treatment period with three consecutive negative sputum examinations. Of 35 patients receiving combined treatment, seven emerged with three consecutive negative sputa at the end of the treatment period. These three consecutive sputum tests covered the final six weeks of the treatment period.

Streptomycin resistant organisms were found to emerge in about half the cases between the 60th and 90th day and by the end of the treatment period all but six patients had developed organisms which were resistant to streptomycin in concentrations of 10 micrograms per cc. Three of the patients whose organisms remained sensitive were in the control group, while the other three were in the SKI group.

Chart I: Cavity Measurements in Streptomycin Group

In the first column the aggregate cavity diameters are tabulated for each patient in the control group before therapy was begun. In the second column are similar measurements taken at the conclusion of treatment. The final column shows the net change in cavity diameter following treatment. Thirteen patients show moderate diminution in cavity size, five show a moderate increase, while five show no change. The average net diminution in cavity diameter for 23 patients is 0.7 cm. per patient.

Chart II: Cavity Measurements in SKI Group

Here is a similar representation of cavity measurements in the SKI group taken before and after treatment. In the third column one case is seen in which the cavities show no change, two cases show a slight increase while all the remaining 32 show varying degrees of diminution in cavity size. The average decrease in cavity measurement in this group is 4.1 centimeters per patient with one patient showing a decrease from 27.2 cm. to 7.1 cm.

CHART II
Cavity Measurements in S.K.I. Group

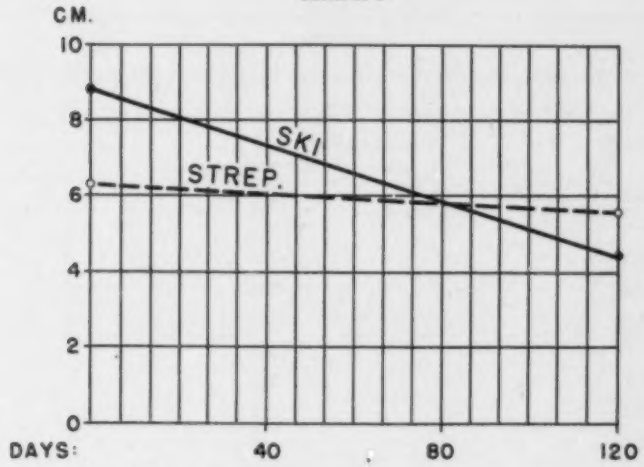
PATIENT	Aggregate Cavity Diameters in Centimeters		Net Change in Diameter During Treatment
	Before Treatment	After Treatment	
S.T.N.	11.2	8.5	−2.7
D.E.L.	5.1	3.9	−1.2
H.E.G.	7.3	4.9	−2.4
E.R.C.	2.6	1.8	− .8
E.T.A.	10.8	8.8	−2.0
D.A.S.	2.9	0	−2.9
S.A.V.	27.2	7.1	−20.1
L.O.D.	11.2	4.6	−6.6
J.E.S.	3.7	2.1	−1.6
W.A.M.	3.9	1.5	−2.4
M.C.G.	6.0	4.0	−2.0
A.R.S.	2.5	0	−2.5
T.H.S.	5.6	3.0	−2.6
L.L.N.	8.2	5.4	−2.8
W.A.S.	6.7	4.2	−2.5
R.E.B.	4.5	3.6	−0.9
E.T.B.	13.3	1.6	−12.7
H.W.D.	3.3	3.7	+0.4
H.E.D.	7.3	5.1	−2.2
D.A.R.	5.5	4.0	−1.5
O.C.K.	8.1	9.7	+1.6
W.A.R.	6.5	0	−6.5
E.L.R.	4.5	2.0	−2.5
C.K.I.	30.0	23.3	−6.7
B.H.I.	5.0	0	−5.0
H.O.W.	3.0	3.0	0
H.A.N.	9.0	2.0	−7.0
G.T.I.	4.8	0	−4.8
P.R.E.	6.2	4.0	−2.2
N.E.L.	24.5	7.5	−17.0
L.M.I.	5.0	3.4	−1.6
R.E.L.	14.0	10.3	−3.7
H.A.R.	11.0	3.5	−7.5
J.J.S.	7.0	5.0	−2.0
M.M.E.	15.0	6.0	−9.0
TOTAL	302.4	157.5	−144.9
AVERAGE	8.6	4.5	− 4.1

Graph I: Cavity Change

This is a graphical representation of the data presented in Charts I and II with the control group beginning at 6.2 cm. before treatment, and ending at 5.5 cm. after treatment.

In the SKI group the average aggregate cavity diameter per patient is 8.6 cm. before treatment, and 4.5 cm. after 120 days or a net decrease in diameter of 4.1 cm.

GRAPH I



AVERAGE AGGREGATE CAVITY SIZE PER PATIENT
(DURING 120 DAY TREATMENT PERIOD)

Chart III: Weight in Streptomycin Group

This chart is a tabular representation of weight changes in the control group, during the treatment period. The first column shows the initial weights, the second column shows the final weights while the net weight changes are recorded in the third column. It is interesting to note that 16 patients show net gains, while seven show losses varying from two to 10 pounds. The total weight gain for 23 patients is 140 pounds, making an average gain of 6.1 pounds per patient, for the 120 days.

Chart IV: Weight in SKI Group

Here is a similar representation of the weights for the group receiving combined treatment. Considerably more consistency is observed with all except two patients showing weight gains. This

group shows a total weight gain of 398 pounds for 35 patients or an average gain of 12.1 pounds per patient for the group.

Statistical Analysis

For the streptomycin group the average or mean reduction in size of cavity is 0.67 cm., the standard deviation is 1.92 cm. and the standard error of the mean is 0.40 cm.

In the SKI group the mean reduction in cavity size is 4.17 cm.,

CHART III

Weight Change During 120 Day Treatment Period in Streptomycin Group

PATIENT	WEIGHT IN POUNDS		Net Weight Change During Treatment
	Before Treatment	After Treatment	
C.H.E.	94	105	+11
S.T.I.	126	120	− 6
W.I.L.	132	126	− 6
M.C.K.	111	120	+ 9
N.A.P.	91	107	+16
C.A.R.	175	187	+12
S.A.T.	124	126	+ 2
O.T.Y.	78	76	− 2
V.A.U.	79	89	+10
E.L.T.	155	169	+14
M.A.S.	104	100	− 4
R.E.T.	90	80	−10
W.O.D.	126	139	+13
B.U.R.	95	96	+ 1
H.U.D.	108	98	−10
S.W.T.	108	120	+12
W.E.N.	133	126	− 7
F.R.H.	105	108	+ 3
G.I.D.	135	168	+33
P.E.S.	151	162	+11
B.O.U.	104	117	+13
C.R.M.	104	113	+ 9
F.K.I.	118	134	+16
TOTAL	2646	2786	+140
AVERAGE	115	121.1	+ 6.1

CHART IV

Weight Change During 120 Day Treatment Period in S.K.I. Group

PATIENT	WEIGHT IN POUNDS		Net Weight Change During Treatment
	Before Treatment	After Treatment	
S.T.N.	153	162	+ 9
D.E.L.	102	112	+10
H.E.G.	132	149	+17
E.R.C.	141	154	+13
E.T.A.	Bed Patient	Bed Patient	Bed Patient
D.A.S.	104	131	+27
S.A.V.	103	117	+14
L.O.D.	95	108	+13
J.E.S.	71	81	+10
W.A.M.	128	140	+12
M.C.G.	Bed Patient	Bed Patient	Bed Patient
A.R.S.	90	93	+ 3
T.H.S.	77	101	+24
L.L.N.	121	135	+14
W.A.S.	186	203	+17
R.E.B.	101	124	+23
E.T.B.	115	144	+29
H.W.D.	137	154	+17
H.E.D.	85	99	+14
D.A.R.	115	134	+19
O.C.K.	120	120	0
W.A.R.	145	165	+20
E.L.R.	145	157	+12
C.K.I.	98	110	+12
B.H.I.	138	141	+ 3
H.O.W.	145	148	+ 3
H.A.N.	128	131	+ 3
G.T.I.	145	148	+ 3
P.R.E.	168	171	+ 3
N.E.L.	76	112	+36
L.M.I.	135	140	+ 5
R.E.L.	111	122	+11
H.A.R.	169	170	+ 1
J.J.S.	132	127	− 5
M.M.E.	137	143	+ 6
TOTAL	4048	4446	398
AVERAGE	122.6	134.7	12.1

the standard deviation 4.6 cm. and the standard error of the mean 0.78 cm.

The difference between the two groups in average reduction of cavity size is statistically significant, the probability of getting a difference as large as that observed through "chance variation" being less than 1 in 1000. The SKI group shows more variability in response (standard deviation 4.6 cm.) than the streptomycin group (standard deviation 1.92 cm.).

The average difference in weight gain is of borderline significance, the probability of getting a difference as large as that observed through "chance variation" being about 3 in 100.

Exudate

Estimations of decrease in exudate for both groups revealed no striking differences between the control and combined groups. In the majority of cases, a marked clearing of exudate was noted.

The initial x-ray film of one of the patients receiving combined therapy is shown in figure 1. Extensive bilateral involvement is seen, with a large, thick walled cavity in the right apex, and multiple cavities on the left.

This x-ray film of the same patient was taken on the 42nd day of treatment (Fig. 2). The large cavity in the right apex is considerably reduced in size, along with the multiple cavities on the left.

A continuation of the same process is seen in figure 3 with the cavity on the right assuming a narrow, elongated contour and most of the cavities on the left closed.



FIGURE 1



FIGURE 2

Figure 4 made from an x-ray film taken 10 days after cessation of therapy, shows a still further diminution in the size of the original large cavity and almost complete obliteration of the cavities on the left.

During the treatment period this patient gained 36 pounds, increasing from 76 to 112 pounds. Her sputum, though positive at the end of treatment, was greatly decreased in amount and she felt well. Unfortunately, her organisms became strongly resistant to streptomycin after the 90th day of therapy.

Follow-Up Examinations

Of the 23 patients treated with streptomycin alone, five have succumbed over a period of nine months. Of the 35 patients in the SKI group, four have died during the same period.

Follow-up x-ray inspections have shown that cavities seen to completely close during the treatment period almost invariably remain closed. Cavities showing partial closure tend to gradually expand following cessation of treatment and in few instances have they returned to their original diameters.

Weight gains, although not always permanent, have tended to remain in the vicinity of that recorded at the end of the treatment period.

Discussion

Speculation as to the underlying mode of action of potassium iodide in tuberculosis still remains largely conjecture. Many have expressed the idea that its beneficial effect in pulmonary tuberculosis may be no more than that produced by its expectorant action. This theory is not borne out by measurement of sputum



FIGURE 3



FIGURE 4

volume from day to day. Instead of an increase in volume most patients exhibited a decrease.

Some observers have felt that many large cavities studied are tension cavities and as such would be expected to fill and empty spontaneously at intervals. This type of cavity could not be completely avoided in a study of this kind. By the same token, many of the cavities observed were thick walled and irregular in outline. The chance of these falling into the tension category is slight. But whatever the underlying mechanism of cavity shrinkage may be, it would seem to follow that any agent which is not harmful and which may promote either temporary or permanent reduction in the size of a cavity during a period of streptomycin administration is beneficial in the overall treatment of tuberculosis with cavitation.

In the group receiving potassium iodide and streptomycin, five patients were observed with small cavities which closed completely. On the other hand, with the emergence of streptomycin resistant organisms after 60 to 90 days, it is reasonable to assume that large cavities cannot close permanently. It seems reasonable, moreover, to visualize the conversion of a case from one in which no hope could be entertained for an operative collapse procedure, to one in which surgical intervention might well prove of lasting value. Under such circumstances the optimum time for surgical collapse therapy would depend upon two main considerations. These are the attainment of maximum improvement in the patient and the avoidance of creating streptomycin resistant organisms. Recent investigations by a group at the Fitzsimmons General Hospital would suggest that the addition of PAS to the treatment regimen might materially delay the emergence of streptomycin resistance.

SUMMARY

A report has been given of the results of treatment in 58 cases of far advanced chronic pulmonary tuberculosis. Twenty-three patients were treated with one gram of streptomycin daily, while the remaining 35 were given combined treatment consisting of streptomycin and potassium iodide. The gradual emergence of streptomycin resistance was noted after the 60th day in all but three cases in each group. Significant radiographic and nutritional changes were noted infrequently in the control group receiving streptomycin alone. In the group receiving streptomycin and potassium iodide considerable improvement was noted both in chest x-ray film changes and in weight. No evidence was found that potassium iodide is harmful in tuberculosis when administered in conjunction with streptomycin. Statistical analysis suggests that the weight variations are of questionable significance, while

the cavity changes appear to be significant. The small cavities in the lungs of five patients receiving streptomycin and potassium iodide closed completely. For this reason it is believed that in selected cases this treatment regimen may avert the need for surgical collapse therapy. In addition, certain far-advanced inoperable cases may be salvaged and rendered more suitable for surgical intervention.

RESUMEN

Se comunican los resultados obtenidos en el tratamiento de 58 casos muy avanzados de tuberculosis pulmonar crónica. Se trató a 23 pacientes con un gramo de estreptomicina al día, mientras que los otros 35 recibieron estreptomicina y yoduro de potasio. Con la excepción de tres casos en cada grupo, en todos los otros se notó el desarrollo paulatino de resistencia a la estreptomicina después de sesenta días de tratamiento. En el grupo de testigos, que recibieron únicamente estreptomicina, no se notaron sino pocos cambios significativos en la radiografía y en el peso. En el grupo que recibió estreptomicina y yoduro de potasio se notó apreciable mejoría tanto en la radiografía torácica como en el peso. No se encontró que el yoduro de potasio es perjudicial en la tuberculosis cuando se administra junto con la estreptomicina. El análisis estadístico indica que las variaciones en el peso tienen un significado dudoso, pero que los cambios cavitarios sí parecen ser significativos. Se cerraron por completo unas pequeñas cavidades en los pulmonaes de cinco pacientes que recibieron estreptomicina y yoduro de potasio. Por esta razón se opina que, en casos seleccionados, ese tratamiento puede obviar la necesidad de emplear la colapsoterapia quirúrgica. Además, se les puede salvar la vida a ciertos casos inoperables muy avanzados que pueden así convertirse en casos más apropiados para la intervención quirúrgica.

RESUME

Les auteurs rapportent les résultats du traitement de cinquante huit cas de tuberculose pulmonaire chronique arrivés à un stade de haute gravité. Vingt-trois malades furent traités par la streptomycine à la dose de un gramme par jour. Les trente-cinq autres reçurent de l'iodure de potassium associé à de la streptomycine. Dans ces deux groupes, chez tous les malades sauf trois, la streptomycino-résistance apparut progressivement après le soixante-troisième jour. Dans le groupe témoin où ne fut utilisé que le traitement streptomyciné, ce n'est que rarement que l'on put noter les améliorations portant sur l'état général et sur les constatations radiologiques. Dans la série de malades traités par la streptomycine et l'iodure de potassium, on constata une amélioration con-

sidérable à la fois sur les aspects radiologiques et sur le poids. Il ne semble pas que l'iodure de potassium puisse être un danger pour les tuberculeux quand il est utilisé en association avec la streptomycine. Sans doute la valeur des variations de poids peut se discuter mais la modification des cavernes prend une valeur démonstrative. Les petites cavités visibles dans les poumons de cinq malades traités par l'association de streptomycine et d'iodure de potassium se fermèrent complètement.

On peut en conclure que dans certains cas choisis, ce traitement peut éviter la collapsothérapie chirurgicale. En outre certains cas trés avancés et inopérables peuvent être de la sorte sauvés et devenir opérables.

REFERENCES

1 Jobling, J. W. and Peterson, W. J.: "A Study of the Ferments and Ferment-inhibiting Substances in Tuberculous Caseous Material," *Exp. Med.*, 19:383, 1914.
2 Barnwell, J. B., et al.: "The Effect of Streptomycin Upon Pulmonary Tuberculosis," *Amer. Rev. Tuberc.*, 56:485, 1947.
3 Woody, E. and Avery, R. C.: "The Combined Effect of Potassium Iodide and Streptomycin on Established Tuberculosis in Guinea Pigs," *Science*, 108:501, 1948.
4 Dye, W. E.: Minutes of the Eighth Streptomycin Conference, U. S. Veterans Administration, November 1949.

Comparative Morphology of Acid-Fast Bacilli*

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Various strains of tubercle bacilli are known to behave differently in regard to their gross colonial morphology, their individual morphologic and tinctorial characteristics, their chemical composition and immunological manifestations, their pathogenicity and their resistance to various chemical substances. While some of the characteristics of the types of acid-fast organisms are well known, others have not been extensively studied. The present study was conducted to ascertain the gross and microscopic morphologic differences of 12 different strains of acid-fast bacilli. The 12 strains intensively studied here during the past year belong to six distinct morphologic types. The cultures used in the study were the following:

1) Avian, isolated from a partridge at Olive View.
2) Virulent bovine, Ravenel strain.
3) Avirulent bovine, BCG.
4) Virulent human (a. H37 Rv; b. O. V. Halstead 113, streptomycin-sensitive; c. O. V. Halstead 595, streptomycin-dependent,[1] d. O. V. Taylor 986, streptomycin-sensitive; e. O. V. Froelich 2908, streptomycin-resistant, f. Froelich 2909, streptomycin-resistant.
5) Avirulent human, H37 Ra.
6) Saprophytes, O. V. Chromogen 3438[2] and O. V. Taylor 2161, PAS resistant.

A variety of culture media and of techniques for examination, were used. Five media have been employed for observation of colonial growth: egg-glycerol medium, sodium oleate agar,[3] Bordet's blood-potato-glycerol agar,[4] tween-albumin fluid medium[5] and serum-synthetic fluid medium.[6] Both light and heavy inoculations were used to afford isolated colonies and confluent growth.

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*This study was supported, in part, by a grant from the National Institute of Health, U. S. Public Health Service, and by grants from the Medical Research Committees of the Los Angeles County Tuberculosis and Health Association and the California Tuberculosis and Health Association.

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TABLE I

Colonial Morphology at Four Weeks Incubation on Glycerol-Egg Media

Type	Color	Shape and Elevation of Surface	Consistency	Size (mm.)	Growth Rate
Avian	cream	raised, usually domed	smooth, moist	1.0	+
Virulent bovine	white	often conical	rough, dry granular	3.0	++
Avirulent bovine	cream	raised, flaky	dry, granular, crumbling	3.0	++
Avirulent human	light tan	raised, seldom spreading	dry, granular, not crumbling	2-3.0	++
Virulent human (streptomycin-susceptible)	light tan	raised, wrinkled spreading	dry, granular, crumbling	3-4.0	+++
Virulent human (streptomycin-resistant)	light tan	raised, wrinkled spreading	dry, granular, crumbling	3-4.0	+++
Virulent human (streptomycin-dependent)	light tan	raised, wrinkled spreading	dry, granular	0.5-1	+
Saprophytes A	cream	raised, no spreading	smooth, moist	0.5-1	++++
B	orange	raised, no spreading	smooth, moist	1-3.0	++++

Heavy inoculations were made with a loop from freshly-growing fluid cultures and light inoculations were prepared in test tubes, bottles or petri dishes by streaking or by spreading the surface of the medium with 1.0 ml of 10^{-4} dilutions of fresh fluid cultures. All cultures were incubated at 37 degrees C., and observed at weekly intervals over periods that varied from eight to 12 weeks. Microscopic observations were made concurrently with cultural observations. At the end of the incubation period, cultures were stored in a refrigerator at 4 to 8 degrees C., for use in later comparative studies.

All strains were studied at different ages by various techniques. Liquid suspensions of living organisms were observed with the ordinary light microscope and the phase microscope. The washed organisms were mounted on collodion or silica films, and examined with an electron microscope. Numerous photographic records were made to supplement the experimental data. The entire culture was inspected with the naked eye and with the aid of low magnification. Fixed smears were also examined with a simple methylene blue stain, a Gram stain and the Ziehl-Neelsen technique.

Differences in colonial morphology are seen with little difficulty while differences in individual morphology are far more difficult to recognize. Many of the characteristics of acid-fast bacilli on various culture media had been described previously for only one or two strains. The findings are summarized in tables I, II, III, IV, V, and VI.

On egg media, the tendency of the virulent tubercle bacillus to produce a dry waxy friable colony which crumbles when rubbed with the inoculating wire, is recognized as a primary diagnostic characteristic. Cultures of avirulent organisms produce firm compact colonies which do not crumble and which usually emulsify more easily in fluid. This characteristic is most pronounced with the saprophytic strains. Avirulent organisms derived from previously-virulent strains of tubercle bacilli (H37 Ra and BCG) produced characteristic avirulent type colonies but did not emulsify easily (Plate I).

On all three solid media, discrete colonies of virulent organisms developed peripheral spreading with very irregular margins during the course of incubation, while avirulent organisms did not. The tendency appeared more slowly in bovine strains which first showed a conical or domed colony and began to spread after the fourth or fifth week of incubation. The spreading tendency in virulent colonies produced from nodular crumbling centers, was most characteristic on Bordet's agar. Avirulent bovine strains often spread at their periphery on egg media, seldom on Bordet's agar

TABLE II

Colonial Morphology at Four Weeks Incubation on Sodium Oleate Agar

Type	Color	Shape and Elevation of Surface	Consistency	Size (mm.)	Growth Rate
Avian	white	flat, spreading	dry	minute	+
Virulent bovine	white	wrinkled, flat, spread, serpentine	dry, waxy	5-8	+++
Avirulent bovine	white	often, raised, no spreading	dry, waxy	minute	+
Avirulent human	cream	raised, no spreading	dry, smooth	1-3	++
Virulent human (streptomycin-susceptible)	cream	wrinkled, flat, spread, serpentine	dry, waxy	5-7	+++
Virulent human (streptomycin-resistant)	cream	wrinkled, flat, spread, serpentine	dry, waxy	5-7	+++
Virulent human (streptomycin-dependent)	cream	wrinkled, flat, spread, serpentine	dry, waxy	0.5	+
Saprophytes A	white	raised	smooth	minute	+
B	orange	raised	smooth	minute	+

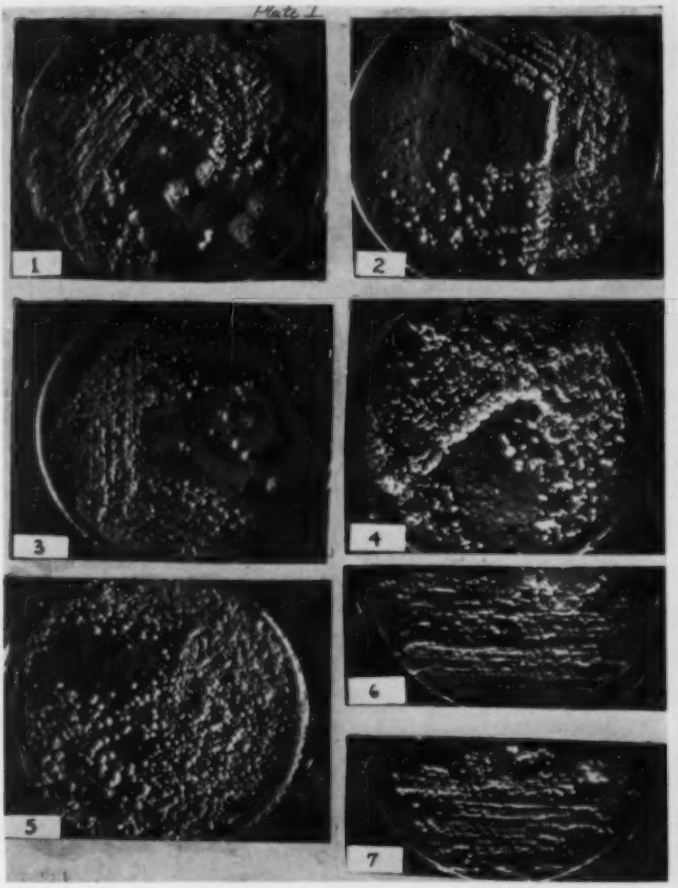


PLATE I

Typical growth of acid-fast bacilli on glycerol-egg media.

1. Virulent human—H37 Rv—at 6 weeks.
2. Avirulent human—H37 Ra—at 6 weeks.
3. Virulent bovine—Ravenel—at 6 weeks.
4. Avirulent bovine—BCG—at 6 weeks.
5. Avian at 6 weeks.
6. Saprophyte A—at 6 weeks.
7. Saprophyte B—at 6 weeks.

TABLE III

Colonial Morphology at Four Weeks Incubation on Bordet's Medium

Type	Color	Shape and Elevation of Surface	Consistency	Size (mm.)	Growth Rate
Avian	cream	raised, no spreading	smooth, moist	0.5	+
Virulent bovine	reddish-brown	spreading, raised, nodular	dry, granular, smooth	2-6	++
Avirulent bovine	reddish-brown	raised, often umbilicated	granular, wrinkled	0.3-1	++
Avirulent human	reddish-brown	raised, no spreading	moist, usually wrinkled	1-3	++
Virulent human (streptomycin-susceptible)	reddish-brown	spreading, raised, nodular center	granular, dry, wrinkled	1-3	++
Virulent human (streptomycin-resistant)	reddish-brown	spreading, raised, nodular center	granular, dry, wrinkled	1-3	++
Virulent human (streptomycin-dependent)	reddish-brown	spreading, raised, nodular center	granular, dry, wrinkled	minute	+
Saprophytes A	cream	raised, glistening	smooth, moist	1-3	+++
B	orange	raised, glistening	smooth, moist	1-3	+++

and older colonies on egg-glycerol medium become noticeably flaky. Flakiness became so pronounced that when bottles or plates were stored in the incubator, a large amount of the growth usually fragmented and fell to the top surface. The chromogenic organism became furrowed and roughened after eight weeks of growth but retained its glistening character.

On sodium oleate agar colonial differences were particularly noticeable between virulent and avirulent tubercle bacilli. Colonies subjected to microscopic examination showed flat, spreading, corded, non-granular, serpentine appearance in all cases with virulent tubercle bacilli, while avirulent organisms presented elevated granular colonies without serpentine orientation. During several series of similar cultures, only virulent organisms showed a satisfactory growth rate, producing moderate to large colonies, while avirulent human organisms, the avian strain and the saprophytes grew very poorly, producing small to minute colonies which usually had to be examined under the microscope for individual characters (Plate II).

Bordet's potato-blood agar medium was used in this study because of the observation of Mishulow that BCG gave characteristic colonies on this medium. Small inocula of the cultures used resulted in the rapid development of colonies. The umbilicated

TABLE IV

Growth at Four Weeks Incubation in Tween-Albumin Liquid Medium

Type	Color	Surface Growth	Submerged Growth
Avian	white	none	smooth
Virulent bovine	white	fine pellicle after 4th week	smooth
Avirulent bovine	white	none	smooth
Avirulent human	white	none	smooth
Virulent human (streptomycin-susceptible)	white	none	smooth
Virulent human (streptomycin-resistant)	white	none	smooth
Virulent human (streptomycin-dependent)	white	none	smooth
Saprophytes			
A	white	none	usually granular
B	gold	none	usually granular

colony of BCG is distinctly characteristic of this strain. Although all colonies on a single plate are not umbilicated, this unusual colony type can always be found during or before the sixth week of growth. Although umbilication was sometimes observed in single colonies on egg media with other types of acid-fast bacilli, it was rarely observed in this study on Bordet's medium in cultures of any other than bovine strains. On Herrold's, as well as Bordet's agar medium only BCG characteristically produced these so-called "doughnut" colonies. Colonies of saprophytic organisms on Bordet's medium remained smooth and glistening at three months incubation despite the obvious lack of visible surface moisture on the medium (Plate III).

Coalescence of cultural growth and the presence of a wet medium surface considerably confused the colonial picture. Confluent growth on all three solid media resulted in a loss of the definite individual characteristics and made the determination of the relative growth rate difficult. In such cases, growth was atypical, the

TABLE V

Growth in Serum-Synthetic Liquid Medium at Four Weeks Incubation

Type	Color	Surface Growth	Submerged Growth
Avian	white	fine, smooth, thin pellicle	fine, granular,
Virulent bovine	cream	uneven small pellicle, slow developing	scant
Avirulent bovine	cream	thick, folded pellicle, little growth on glass	scant
Avirulent human	cream	thick, folded pellicle, growth on glass	scant
Virulent human (streptomycin-susceptible)	cream	thin, corded pellicle, growth on glass	scant
Virulent human (streptomycin-resistant)	cream	thin, corded pellicle, growth on glass	scant
Virulent human (streptomycin-dependent)	cream	thin, corded pellicle, growth on glass	scant
Saprophytes			
A	white	thick, smooth pellicle, no growth on glass	moderate, granular
B	orange	thick, smooth pellicle, no growth on glass	moderate, granular

normal surface appearance and consistency of the colonies was lost and visible growth occurred very slowly. This was particularly noted with growth on Bordet's medium. Isolated colonies growing on a wet surface during one of the original growth series showed almost entirely a morula or mulberry type colony which was small and afforded little distinction between the strains studied. Since dryness and consistency are primary characteristics, interference with their development by wet media surfaces is to be avoided.

Some differential features were also noted on the liquid media used in this study. Tween-albumin medium allowed the rapid growth of *Mycobacteria* from small inocula; growth was submerged, occurring as a flat layer on the bottom of the fluid column. The bovine culture produced a thin pellicle at four weeks in all culture series, whereas all other cultures produced a pellicle

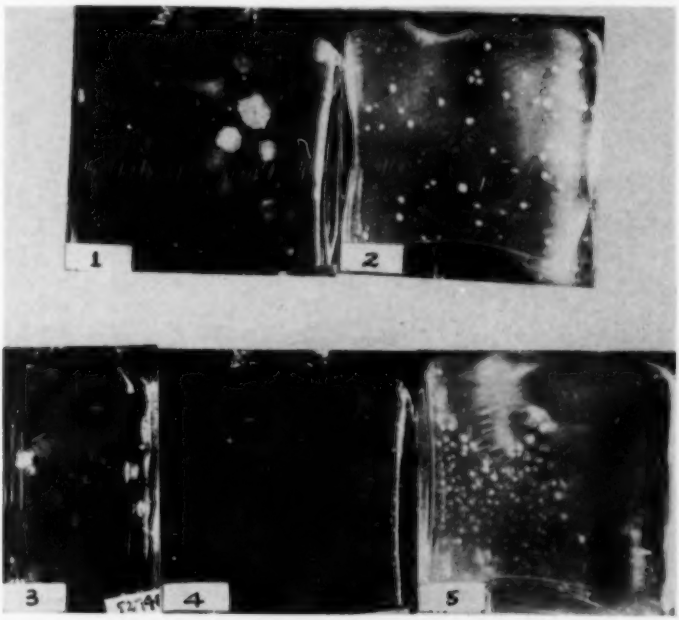


PLATE II

Typical growth of acid-fast bacilli on sodium oleate agar.

1. Virulent human—H37 Rv—at 8 weeks.
2. Avirulent human—H37 Ra—at 8 weeks.
3. Virulent bovine—Ravenel—at 8 weeks.
4. Virulent human—H. 595, streptomycin dependent—at 8 weeks.
5. Saprophyte B at 8 weeks.

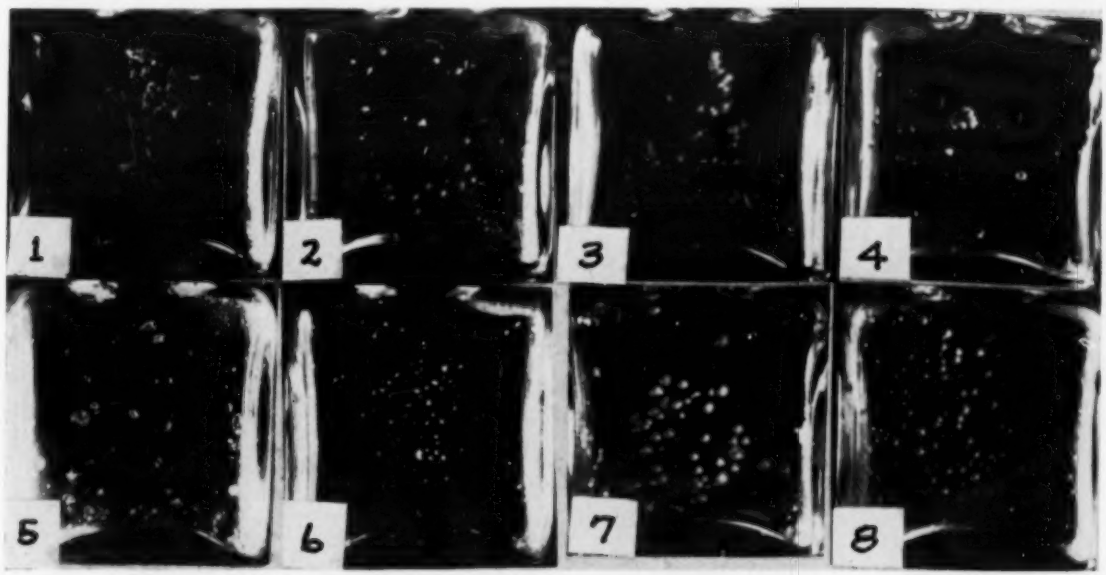


PLATE III

Typical growth of acid-fast bacilli on Bordet's medium.

1. Virulent human—H37 Rv—at 8 weeks. 2. Avirulent human—H37 Ra—at 8 weeks. 3. Virulent bovine—Ravenel—at 8 weeks. 4. Virulent bovine—Ravenel—at 8 weeks (medium surface is very moist). 5. Avirulent bovine—BCG—at 8 weeks. 6. Avian at 8 weeks. 7. Saprophyte A at 8 weeks. 8. Saprophyte B at 8 weeks.

only after prolonged incubation, perhaps when the surface-active agent was exhausted.

On serum-synthetic medium, the virulent human type strains produced thin corded pellicles which grew from 5 to 7 mm. up the sides of the glass tubes, while the avirulent human organisms gave a thick, granular pellicle which covered the surface of the fluid column but did not grow up the glass. The avirulent bovine strain showed this same type of thick folded granular pellicle. Bovine (Ravenel) organisms did not grow as luxuriantly as other strains. Its pellicle was slower in development and did not cover the fluid column, and it showed several areas of uneven thickness, so that the growth had a plaque-like appearance. The saprophytes showed both considerable granular submerged growth and heavy, thick, smooth pellicles. Avian bacilli produced a thin surface growth with a fine granular sediment. With the avian strain, moderate deep growth always occurred before the pellicle was completely formed.

Living unstained tubercle bacilli suspended in liquid media under cover slips and observed with high dry and oil immersion objectives under reduced illumination appeared indistinct. No motility was present but individual morphology could not be clearly recognized because of Brownian movement and poor definition. Un-

TABLE VI

Individual Morphology of Acidfast Bacilli

Type	Length	Width	Curvature	Beading on AF Stain	Bipolar Nucleoids	Multiple Nucleoids	Fusiform Swellings	Branching
Avian	2.5	.1	+	+	++	±		±
Virulent bovine	2.5-3	.2	+	+	++	±		
Avirulent bovine	2.5-3	.2	+	+	++	++		
Avirulent human	2.5-3	.2	+	+	++	±		
Virulent human (streptomycin susceptible)	3.5-4	.1	++	+	++	±		
Virulent human (streptomycin resistant)	3.5-4	.1	++	+	++	±		
Virulent human (streptomycin dependent)	3.5-4	.1	++	+	++	±		
Saprophytes								
A	2.5-6	.1-.2	+	+	++	++	+	
B	2.5-6	.1-.2	+	+	++	++	+	±

stained dried films gave even less information. Using the darkfield microscope, the size and shape of the bacilli could be discerned but internal structures were not clearly shown.

Phase microscopy is a relatively new method of examination by which structures of inherently low contrast in living organisms and other transparent materials may be observed. To do this, the object is transilluminated obliquely by light passing through an annular diaphragm under the condenser lens, and a ring of light absorbing and diffracting material is placed in the focal plane of the objective. The retardation of the light passing through the diffraction plate causes particles of different refractive index to appear brighter or darker than the background. Varying types and degrees of contrast may be obtained with different arrangements and values of light transmission and diffraction in the diffraction plate.

At the beginning of the study, darkfield illumination and phase microscopes were compared. The phase microscope was used in later work because it allows greater resolution than the darkfield microscope while giving excellent contrast. Bright medium contrast and low contrast 1.8 mm. oil immersion objectives were used for all observations and photomicrographs. The phase microscope allows better photography than the darkfield microscope.

The unstained organisms of different types revealed differences in size and shape similar to those observed with stained preparations. Internal structural features, however, were more consistent on repeated examinations. Dense bodies, resembling nuclear aggregates, were clearly seen within the cell. These bodies were generally round and bipolar. Only occasionally did the nucleoids of tubercle bacilli swell the cell. The saprophytic organisms, however, often showed dark fusiform bodies which swelled the cell to twice its diameter. BCG and the saprophytes frequently showed multiple granulations, with four or five granules scattered throughout the length of the bacilli. Fusiform swellings and a high concentration of cells with multiple granules were not observed in any other organisms. Small rods, probably consisting of the so-called "dust particles" seen on stained films, morphologically resembled the larger forms, and often had small bipolar granules. Examination of intact living cells from three days to 12 weeks of incubation did not disclose motility, flagella, capsules or spores.

Preparation of the tubercle bacillus for examination with the electron microscope presented difficulties, because of the tendency of the organisms to form small clumps, even in tween-albumin medium and because of the necessity for a field free from crystals and artifacts. Liquid cultures were centrifuged for 15 minutes at 1500 r.p.m., the supernatent fluid discarded, and the organisms

washed in sterile saline solution from three to eight times. The saline solution was removed by washing once with distilled water. The organisms were then resuspended in distilled water and shaken to break up the clumps. The heavier material was allowed to settle and the supernatant fluid, containing mostly single organisms, was mounted on both collodion and quartz films. By this technique, relatively clean preparations could be made. The specimens were examined without any fixation or staining. Greater difficulties were found in making films from solid media because

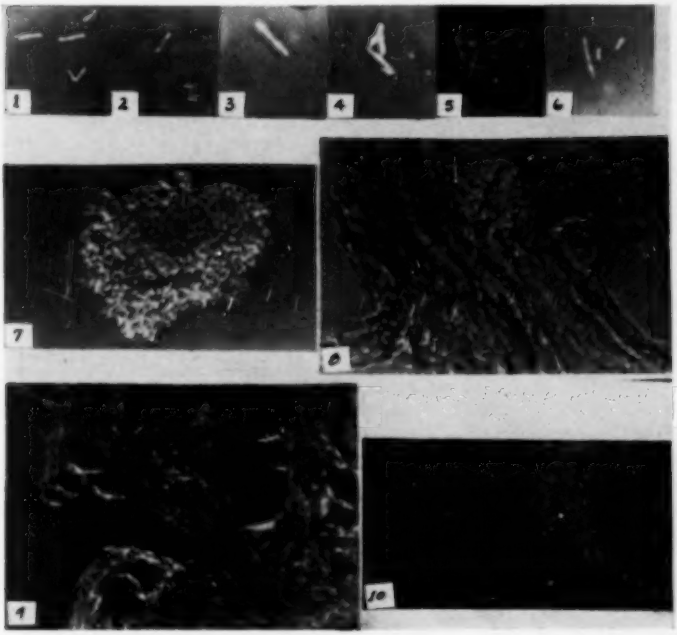


PLATE IV

Morphology of acid-fast bacilli with phase microscope preparations in fluid media using bright-medium 1.8 mm. oil immersion objective. Exposure 60 seconds on 35 mm. Pan X film.

1. Avirulent human—H37 Rv—showing bipolar nucleoles.
2. Virulent human—O.V. Halstead 113—showing bipolar nucleoles.
3. Saprophyte A.
4. Saprophyte A.
5. Saprophyte A.
6. Saprophyte B.
7. Avirulent human—H37 Ra.
8. Virulent human—H37 Rv.
9. Virulent bovine—Ravenel.
10. Saprophyte B.

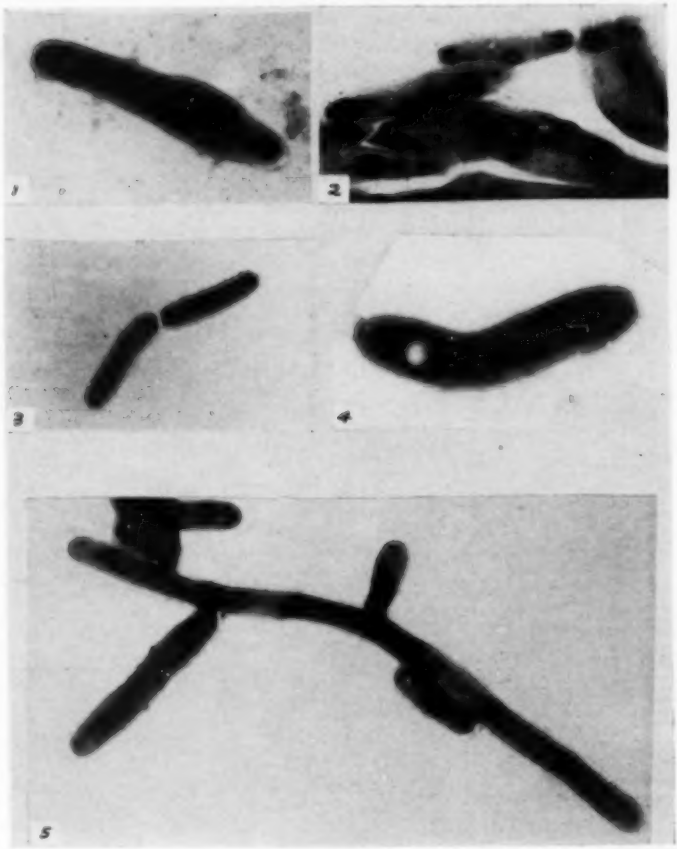


PLATE V

Electron microscope photomicrographs.

1. Virulent human—H37 Rv—at five days incubation, showing slightly swelled cells.
2. Virulent human—H37 Rv—at six weeks incubation, showing bipolar nucleoids, and small nuclear bodies.
3. Avirulent human—H37 Ra—at five days incubation, showing typical bipolar nucleoids.
4. Avirulent bovine—BCG—at twelve weeks incubation, showing small multiple nuclear bodies and vacuolation.
5. Avian strain—at five days incubation in tween-albumin medium, showing a branching form.

of the large number of artifacts in the films and the greater age of the cultures which usually revealed many ghost cells.

The electron microscope confirmed and amplified the findings of the phase microscope. The bacilli had a rather homogeneous cytoplasm and the dense round bodies, usually bipolar in arrangement, were conspicuous. In most cells, particularly in preparations from fluid media, there were two such nucleoids, but in older organisms examined after eight to 12 weeks of incubation, several minute granules could also be seen. In films of young cultures on fluid media, prepared at five days of incubation, when an increase of growth is first observed by nephelometric techniques, very few nucleoids were found and the cells usually showed no internal organization. The saprophytes showed occasional intracellular bodies which swelled the cell and each film showed a few long filamentous rods with three to four granules. With the electron microscope, older cells often showed round vacuoles. No evidence of flagella or spores was found (Plate V).

Clear zones were sometimes seen around all or part of the cells, bordered by fine dense lines, or gradually blending into the background, but the clear zones were considered to be due to retraction of cell material from the supporting collodion membrane resulting from the drying and evacuation of the film or the heat of the electron beam rather than the result of preexisting capsules or different distribution of materials of lighter electron density in the intact organism. Dense spots or fragments of irregular size or shape were seen clinging to the border or scattered over the film especially in the vicinity of the cells, but these were rare or absent on silica films or in cleaner collodion preparations and were due to foreign crystal deposits and other artefacts unrelated to the bacilli themselves (Plate VI).

Washed preparations of five day cultures of the avian and chromogen strains in tween-albumin medium showed branching forms when examined with the electron microscope. Each organism produced one or two racquet-like branches from a long slender filamentous-type cell.

Thin smears lightly stained with methylene blue showed intracellular structures more easily than did the denser, more tedious Gram stain. Although the organisms at all stages exhibited a considerable variation in length and often in width, virulent organisms were longer and more slender than avirulent types. Virulent human organisms were generally long and slender, often with tapered ends and frequently curved and more uniform, with less tendency to form very short rods or filamentous forms. Avirulent organisms were shorter, usually thicker, and frequently showed considerable variation in length, from short coccobacillary rods

which have been confused with extracellular granules, to long crooked slender forms. Generally, the virulent human organisms had an average length of 3.5 to 4 microns and width of 0.1 micron, while the average avirulent bovine and avirulent human organisms were 2.5 to 3.0 microns in length and 0.2 micron in thickness.

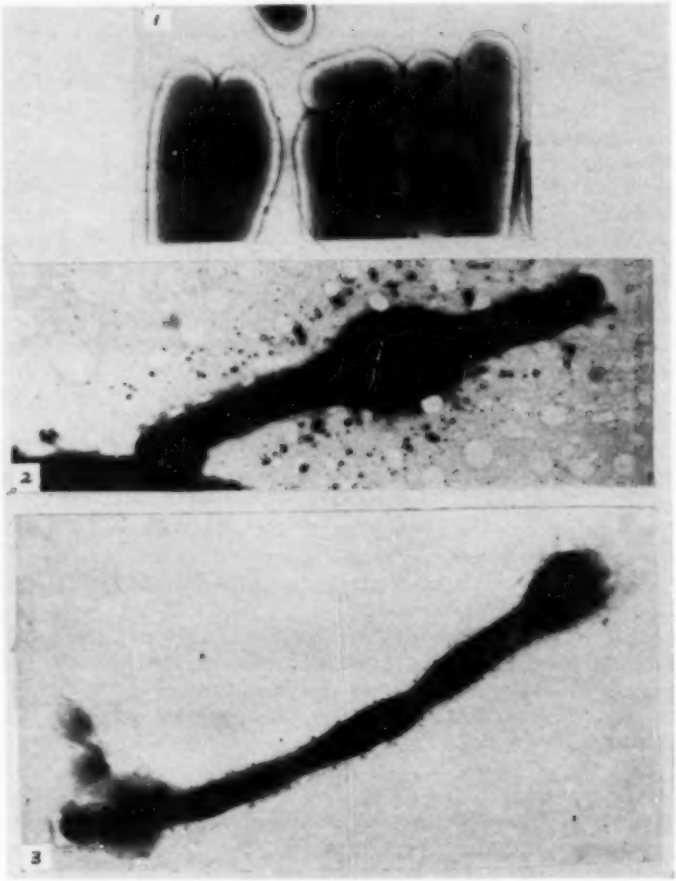


PLATE VI

Electron microscope photomicrographs.

1. Saprophyte A—at five days incubation, showing short uniform cells.
2. Saprophyte B—at twelve weeks incubation, showing large fusiform body and small nucleoid.
3. Saprophyte B—at twelve weeks incubation, showing long swelled rod.

Saprophytic organisms showed a wide variation of individual morphology, sometimes developing long filamentous forms in old cultures but usually they appeared to be short plump rods. The avian organisms generally were most uniform in individual appearance, the average length being about 2.5 microns.

Methylene blue stained smears often showed the presence of small deep blue-black intracellular bodies in light blue stained bacilli. These dense bodies were usually two to a bacillus, bipolar in position, and occasionally appeared to swell the bacilli. They were seen in all types of acid-fast organisms of all ages.

The Gram stain generally revealed the same individual morphology, with the same size and shape of the bacilli, as did the methylene blue stain, and a similar internal structure. The bipolar nucleoid bodies were always an intense dark purple, but the remainder of the bacterial substance varied from pink to purple, even in the same organism. No consistent differences were observed, with the Gram stain, in the tinctorial reaction of the nucleoid masses or the remainder of the bacillary material, between the various types of acid-fast organisms nor between cultures of different ages nor on different kinds of media.

On acid-fast staining, the length and thickness of individual organisms and the cell arrangement is clearly seen but many of the bacilli exhibited swellings and beading not seen in the other stains nor in unstained preparations from the same culture at the same time. Our observations confirmed those of Yegian and his co-workers[7] that multiple beading and some types of swollen forms commonly observed in acid-fast stained preparations are the result of improper technique and faulty reagents. The swellings and beads appeared to be more strongly acid-fast than the remainder of the individual cell but the granules seen in some stained preparations, by virtue of their increased density often disappeared when the acid-fast stain was repeated and the organisms then appeared smooth and evenly-stained. The appearance of these elements did not seem to be entirely a function of the age of the cultures though they were seen more often in old than in young cultures. Usually, only two, or perhaps three, dense bodies were seen in the majority of the cells, when stained with methylene blue or examined with the phase microscope.

When the same preparations were acid-fast stained, however, many of the cells were beaded or contained deep bluish-black or red granules which appeared to swell the organism. At the same time, many of the organisms which exhibited dark bodies in unstained preparations failed to show any granules at all with the acid-fast stain and were a smooth, even, deep pink stain.

When stains of the acid-fast saprophytes were prepared at six

to eight weeks of incubation, large fusiform bodies and bizarre filamentous form were seen, as well as some beading. These structures resembled those seen with the electron microscope and the phase microscope, but no intracellular bodies similar to the beaded forms seen with the acid-fast stain could be detected by the other methods. With most of the virulent and avirulent organisms other than the saprophytes, only an occasional slightly swollen bacillus could be seen with the electron microscope.

Although they could be detected by other means, lightly-stained methylene blue smears and phase microscope preparations most clearly revealed the serpentine type of cell arrangement observed by Dubos and others[6] in the H37 Rv strain of Mycobacterium tuberculosis. All virulent human and bovine bacilli showed this cording in all media except the tween-albumin fluid medium in which the surface-active agent inhibited about 90 per cent of this type of orientation. The cells were arranged in long chains and lay side by side, producing long swirls of closely packed organisms. Avian, avirulent human and bovine tubercle bacilli and the saprophytes did not show this type of orientation. Preparations of these organisms exhibited tightly-packed granular masses of rods with no orientation. A few of these strains showed a slight tendency to a serpentine orientation, but this was not a constant finding (Plate IV).

There appeared to be no differences either in gross or microscopic morphology between streptomycin-susceptible parent strains and streptomycin-resistant and dependent strains recovered from the same patients. The streptomycin-dependent organisms studied appeared to be similar in all characteristics to the parent susceptible strain with the exception of variation in colony size due to the interference with growth rates by the presence or absence of streptomycin. In suitable concentrations of this antibiotic, this strain grew more slowly, though the colonies were identical morphologically and the microscopic pictures showed no change.

SUMMARY

A morphological study, both cultural and microscopic, was conducted, using ten strains of virulent and avirulent tubercle bacilli and two acid-fast saprophytic organisms isolated from sputum. The organisms were studied on five different media and preparations were made for microscopic examination using the following techniques: wet preparations with the ordinary light microscope, darkfield microscope and phase microscope; unstained dried films with ordinary light microscope and electron microscope; and fixed dried films stained with methylene blue, Gram stain and Ziehl-Neelsen stain.

At least half a dozen different forms of acid-fast bacilli were clearly distinguished by colonial morphological characteristics. Virulent human types were distinguished from all other organisms by their dry, crumbling, spreading colonies on egg media and Bordet's agar, their characteristic large serpentine colonies on sodium oleate agar, and thin corded pellicles which grew up the walls of the tube in the serum-synthetic medium. The avirulent human type produced granular colonies with no crumbling on egg media and Bordet's agar and a small non-serpentine colony on sodium oleate agar. Thick folded pellicles in serum-synthetic media characterized this organism. The virulent bovine type also produced serpentine growth on sodium oleate agar and spreading crumbling colonies on egg media and Bordet's medium. BCG always produced flaky growth on egg media and characteristic umbilicated colonies on Bordet's medium. Avian organisms showed smaller colonies with little spreading and usually, a smooth surface. The saprophytes always produced smooth shiny colonies on all solid media and heavy smooth pellicles on serum-synthetic medium. Only virulent organisms produced spreading on egg media and Bordet's agar and serpentine flat spreading colonies on sodium oleate agar. On the latter medium, only virulent organisms produced satisfactory growth, the avirulent types growing very poorly.

Microscopically, the serpentine or corded arrangement of virulent tubercle bacilli contrasted sharply with the diffuse granular appearance of avirulent strains. Dense intracellular bodies, often bipolar, seen in all strains of acid-fast bacilli corresponded in form and position to similar structures in electron microscope films and in methylene blue stained smears. These nucleoids appeared to be quite different from the beading or granules often seen in acid-fast stained smears. Large fusiform swellings were seen only in saprophytic strains though small bulges occasionally appeared in other acid-fast bacilli. Saprophytes and avian tubercle bacilli also occasionally showed long filamentous rods and forms suggesting branching growth. Neither gross colonial nor microscopic morphological, nor tinctorial differences were noted between human type tubercle bacilli which were resistant to, or dependent on, streptomycin and their parent susceptible strains.

Further study, including forty other strains of acid-fast bacilli, has generally confirmed the observations reported here. Of five strains received as BCG, however, two resembled the avirulent human, rather than the avirulent bovine type described. Among a dozen additional saprophytic acid-fast strains received, two more types were noted. Saprophyte type C, including M 607, M. ranae, M. smegmatis, and several cultures labelled M. leprae, appeared buff, wrinkled, pasty, moist, and rapidly growing on solid media, with cream colored abundant surface and sub-

merged growth on liquid media. Saprophyte type D, including M. phlei and another labelled M. leprae, were yellow to orange, flat or nodular, spreading, waxy, large and rapidly growing colonies on solid media, with serpentine arrangement on sodium oleate agar medium, and with yellow flaky pellicles and scanty granular submerged growth in liquid media.

RESUMEN

Se llevó a cabo un estudio morfológico, tanto cultural como microscópico, usando diez cepas de bacilos tuberculosos virulentos y avirulentos y dos organismos saprofíticos ácidorresistentes aislados del esputo. Se estudiaron los organismos en cinco medios diferentes y se hicieron preparaciones para el examen microscópico usando las técnicas siguientes: preparaciones húmedas con el microscopio de luz ordinaria, el microscopio de campo oscuro y el microscopio de fase; películas secas no teñidas, con el microscopio de luz ordinaria y el microscopio de electrón y frotes secos fijos teñidos con el azul de metileno y las soluciones colorantes de Gram y de Ziehl-Neelsen.

A base de las características morfológicas coloniales se distinguieron claramente por lo menos media docena de formas diferentes de bacilos ácidorresistentes. Se distinguieron los tipos virulentos humanos por sus colonias secas, desmenuzadas y extendidas en el medio de huevo y en el agar de Bordet y sus características colonias grandes y serpentinas en el agar con oleato de sodio y las finas películas acordonadas que crecieron sobre las paredes del tubo en el medio de suero sintético. El tipo humano avirulento produjo colonias granulosas no desmenuzadas en el medio de huevo y en el agar de Bordet, una pequeña colonia no serpentina en el agar con oleato de sodio y películas características, gruesas y dobladas, que no crecieron sobre las paredes del tubo. El tipo bovino virulento también produjo un crecimiento serpentino en el agar con oleato de sodio y colonias desmenuzadas y extendidas en los medios de huevo y de Bordet. El BCG siempre produjo un crecimiento escamoso en el medio de huevo y características colonias umbilicadas en el medio de Bordet. Los organismos del tipo de aves mostraron colonias más pequeñas que poco se extendieron y que generalmente tenían una superficie lisa. Los saprofitos siempre produjeron colonias lisas y lustrosas en todos los medios sólidos y películas lisas y pesadas en el medio de suero sintético. Solamente los organismos virulentos produjeron esparcimiento en el medio de huevo y en el agar de Bordet y colonias serpentinas, planas y esparcidas en el agar con oleato de sodio. En este último medio sólo los organismos virulentos produjeron un crecimiento satisfactorio, los tipos avirulentos crecieron muy mal.

Microscópicamente, el arreglo serpentino o acordonado de los bacilos tuberculosos virulentos fue muy diferente del aspecto difuso

y granuloso de las cepas avirulentas. Los cuerpos intracelulares espesos, y a menudo bipolares, que se encuentran en todas las cepas de bacilos ácidorresistentes corresponden en forma y posición a estructuras semejantes que se ven en películas con el microscopio de electrón y en frotes teñidos con el azul de metileno. Estos nucleoides parecieron ser muy diferentes de las bolitas o gránulos que frecuentemente se ven en frotes teñidos con el colorante ácidorresistente. Solamente se vieron hinchazones grandes y fusiformes en las cepas saprofíticas, aunque pequeñas combas aparecieron de vez en cuando en otros bacilos ácidorresistentes. Los bacilos tuberculosos saprofíticos de tipos de aves también mostraron, ocasionalmente, varillas largas y filamentosas y formas que sugerieron crecimiento ramificado. No se notaron diferencias coloniales en bruto, morfológicas microscópicas o tintóreas entre los bacilos tuberculosos de tipo humano que eran resistentes a la estreptomicina o dependientes de la estreptomicina y las cepas susceptibles que las antecedieron.

RESUME

Les auteurs ont fait une étude de l'aspect que présente certains bacilles soit sur les milieux de culture soit à l'examen microscopique. Ils ont utilisé dans ce but dix souches de bacilles tuberculeux et avirulents et deux germes acido-résistants saprophytes. Les microbes furent étudiés sur cinq milieux différents et des préparations furent faites pour l'examen microscopique. Tous les procédés de coloration et d'examens microscopiques y compris le microscope electronique furent utilisés.

Finalement une demi-douzaine de formes différentes de bacilles acido-résistants furent clairement individualisés par leurs caractères morphologiques. Les bacilles humains virulents se distinguaient de tous les autres germes par leurs colonies sèches, filtrables et extensives. Quand elles étaient cultivées sur les milieux à l'oeuf ou sur le milieu à la gélose de Bordet. Leurs colonies abondantes et ondulées sur gélose à l'oléate de sodium et leurs minces pellicules en forme de cordon qui se développent sur les parois du tube sont caractéristiques de leur culture en milieu synthétique au sérum. Le type humain avirulent forme des colonies granuleuses non friables sur les milieux à l'oeuf et la gélose de Bordet. Sur gélose à l'oléate de soude les colonies sont petites et non ondulées. Les pellicules en sont épaisses, repliées et ne s'étendent pas le long du tube. Les germes bovins virulents forment également des cultures ondulées sur gélose à l'oléate de soude et des colonies exubérantes et friables sur les milieux à l'oeuf et sur le milieu de Bordet. Le BCG pousse en flaques sur les milieux à l'oeuf et donnent sur le milieu de Bordet des colonies ombiliquées caractéristiques. Les

bacilles aviaires constituent des colonies plus petites, peu exubérantes et habituellement à surface lisse. Les saprophytes se disposent toujours sur milieux solides en colonies lisses et brillantes et produisent sur milieu synthétique au sérum des pellicules extrémement lisses. Seules les bactéries virulentes produisent des colonies exubérantes sur milieux à l'oeuf et sur milieux de Bordet, et de riches colonies plates et ondulées sur gélose à l'oléate de soude. Sur ce dernier milieu, seuls les germes virulents se développent favorablement, les souches avirulentes ont un développement extrèmement pauvre.

Microscopiquement, il y a un contraste frappant entre la disposition ondulée ou en cordon des bacilles tuberculeux virulents et l'aspect dispersé et granuleux des souches avirulentes. Des corps intra-cellulaires souvent bipolaires existent sur toutes les souches de bacilles acido-résistants. Ces corps sont très différents des granules que l'on constate fréquemment sur les frottis de bacilles acido-résistants. Ce n'est que dans les souches saprophytes que l'on voit de volumineux renflements fusiformes; toutefois on peut voir dans certains cas de petits gonflements dans d'autres bacilles acido-résistants. Les saprophytes ainsi que les bacilles tuberculeux aviaires se présentent parfois sous forme de longues expansions filamenteuses et prennent un aspect ramifié. Aucune différence ni dans l'aspect des colonies ni dans les caractères morphologiques ni dans la coloration n'a pu être décelée dans les bacilles tuberculeux humains selon qu'ils fussent streptomycino sensibles, streptomycino résistants ou streptomycino dépendants.

REFERENCES

1 Doane, E.: "A Streptomycin-dependent Tubercle Bacillus," Paper read before the Los Angeles Trudeau Society, February 28, 1950.

2 Wenkle, W., Loomis, R. and Jarboe, J.: "Chromogenic Acid-fast Bacilli," *Amer. Rev. Tuberc.*, 17:385, 1948.

3 Dubos, R. and Middlebrook, G.: "Media for Tubercle Bacilli," *J. Exper. Med.*, 88:81, 1948.

4 Bordet, J. and Gengou, O.: "Le microbe de la coqueluche," *Ann. Inst. Past.*, 20:731, 1906.

5 Dubos, R. and Davis, B.: "Factors Affecting the Growth of Tubercle Bacilli in Liquid Media," *J. Exper. Med.*, 83:409, 1946.

6 Youmans, G. P.: Chairman, Report of the Laboratory Subcommittee, etc., *Amer. Rev. Tuberc.*, 61:274, 1950.

7 Yegian, D. and Baisden, L.: " Factors Affecting the Beading of the Tubercle Bacillus Stained by the Ziehl-Neelsen Technique," *J. Bact.*, 44:667, 1942.

8 Middlebrook, G., Dubos, R. and Pierce, C.: "Virulence and Morphological Characteristics of Mammalian Tubercle Bacilli," *J. Exper. Med.*, 86:175, 1947.

Discussion

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Mr. Will Bogen has made a praiseworthy report on the variability of the colony morphology of Mycobacterium tuberculosis. Among many features, he has mentioned some important marks of virulence, such as, the rough and granular types as opposed to the smooth and moist types. However, that distinction is not always sharp as there are some exceptions to both. Different media also produce different characteristics. The same is true of many of the other changes in colony characteristics.

All in all, there are about as many exceptions as there are rules, and colony morphology is no certain criteria of the virulence or avirulence of any particular strain of tubercle bacilli.

Nevertheless, it is necessary to attempt to see if the secret of virulence or avirulence can be found. One that seems to be rather consistent is the association of chromogenesis with avirulence. Yellow or orange colonies generally possess little virulence, yet there are exceptions to this rule. Most chromogens are considered as saprophytes, and probably are, but I am not so sure there are not exceptions. I have seen an abundant growth of characteristic white rough colonies of typically appearing tubercle bacilli turn yellow by simply uncorking the bottle and exposing it to oxygen. Upon inoculation into guinea pigs the organisms produced tuberculosis in the animals. Culturing from the lesions again the colonies were white but turned yellow once more, on standing. I have also seen mixed yellow and white colonies. For the reasons given, I doubt if we are justified in labelling all chromogens as saprophytes. Most chromogens are avirulent but I wonder if some may not represent a degradation of virulence of typical tubercle bacilli rather than saprophytic contaminations.

The morphology of the tubercle bacillus itself has been one of my interests of long standing. I must say that there has been a tendency of recent years to discount much of the observations on morphology of earlier work. I think this is unfortunate. Nowadays, the media are usually of such qualities that strains grow pretty true to type and do not reveal much change. The growth on poor media or in a living host, however, offers a much greater opportunity for abnormal forces to act on the microorganisms and produce a result in the variations described by many of the earlier workers whose work cannot all be brushed aside as poor technique. To label all studies of that nature as erroneous or due to poor technic, without more proof, is scientific myopia.

The rule is to find a smooth, slightly curved bacilli of a certain size, with the chromatin evenly distributed so that it stains uniformly. As bacilli are subjected to unfavorable environment, however, there are changes that take place within the nuclear material. The most obvious one is the formation of granules of various sizes. The bacillus, as a unit, may go on to death, but life persists many times in the granules which may revert to bacilli again upon proper culture. Sometimes the changes are extreme and unusual forms may appear at first. Very small bacilli may develop, with typical bacilli growing later. On three occasions I have seen granules grow into large globoid bodies which assume the shape of doughnuts, or, more properly, hollow spheres with bacilli forming or sprouting in various ways into horseshoe shapes, comma shapes, and other bizarre forms. To disregard these changes is to "fail to see the forest for the trees." The significance of the changes described is not yet clear, but it is unscientific to shut ones eyes and say they do not happen. Who of us have seen the tubercle bacillus in all its possible environments?

It is possible that the explanation of sarcoidosis may be hidden in such phenomena. Although I have not often seen the changes described, they have been seen enough to affirm that the tubercle bacillus may at times be weakly acid-fast or even non-acid-fast and it may, under certain conditions, assume granular shapes which may be restored to the normal bacillary morphology by growing in proper media. The most important point I wish to make is that we do not yet know all about the tubercle bacillus and its morphological changes. Just as Dr. Bogen has shown that colony morphology is still enigmatic, there are still unknown features of the tubercle bacillus.

Streptomycin and Artificial Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis*

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Infectious processes within the body characterized by the formation of purulent exudates should be adequately drained if rapid clearing of the lesion is to be expected, and this should be accomplished early if irreparable changes in the tissues are to be prevented. Due to the peculiar anatomy of the lung, this basic principle of drainage is of increasing importance since it may be much harder to accomplish after the normal physiological mechanism of drainage has been damaged through the formation of productive, fibrotic, or cavitary changes within the lung. The earlier treatment is started, therefore, for the specific purpose of instituting drainage of infectious exudates from the lung and bronchial tree, the greater will be the prospect for early arrest or cure of the disease. Delay may mean failure of the treatment.

It has been demonstrated, for example, that the recurrence of lung abscess is not infrequently seen because of delay in the institution of drainage. This is due to the development within the lung of permanent fibrotic changes which prevent adequate cleansing of the infectious exudates from the involved area through a partial blockage of the bronchi by peribronchial contraction on the one hand, and a lessened mobility of the lung on the other. Because it is now realized that adequate drainage may not be attained, excision of the pathological process is frequently practiced. This holds true, not only for pulmonary abscess, but also for pulmonary tuberculosis.

In pulmonary tuberculosis, partial blockage of the bronchus by peribronchial fibrosis or endobronchial disease, or a loss of mobility of the lung as in complete consolidation with or without cavity formation are conducive to the retention of infectious exudates with resulting progression of the disease. This is entirely mechanical and has nothing to do with the immunity of the individual.

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*From the Tuberculosis Service, Veterans Administration Hospital, Downey, Illinois. Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the author.
Read before the Sixteenth Annual Meeting of the American College of Chest Physicians, San Francisco, California, June 23, 1950.
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It is not uncommon for example, to observe a clearing of a tuberculous process in one part of the lung with progression of the disease in another part of the same lung. We have all seen bronchogenic spreads to the base of the contralateral lung from an active apical lesion. Such basal spreads may often clear while the original upper lobe lesion remains unchanged. Too, it is frequent that chronic progressive tuberculosis may be seen to exist in an advanced stage over a period of many months in one lung, whereas little or no disease can be demonstrated roentgenologically in the other. In my opinion these so-called phenomena can not be explained except on the basis of adequate drainage on the one hand and inadequate drainage on the other.

This paper will deal with artificial pneumoperitoneum and streptomycin in the treatment of pulmonary tuberculosis, and the role they play in the restoration of the drainage mechanism of the lungs and bronchial tree. The patients in this series have been treated with pneumoperitoneum, but without surgical paralysis of the phrenic nerve.

In previous publications by the author since 1938 it has been pointed out that by simply elevating the foot of the bed of patients with disease located chiefly in the upper part of the lung, and who had great difficulty in raising their sputum, ease of expectoration followed shortly thereafter. In this position, the rise of the diaphragm results in a relaxation of those portions of the lungs situated in the apices of the various lobes where tuberculosis usually develops and progresses. In addition, the upper parts of the lobes situated in the costovertebral gutter where comparatively little motion normally exists now become more mobile and function similarly to the remainder of the lung with more vigorous lengthening and shortening of the bronchial tree. This results in better drainage from these areas as indicated by ease of expectoration.

Following this, other symptoms such as cough, fever, failure to relax with inability to rest and shortness of breath become less severe or entirely disappeared in 85 per cent of the cases. Clearings on x-ray films occurred in 65 per cent of the cases, and 34 per cent of the patients with cavities closed them. It was concluded that retention of infectious exudates in the apices of the lobes due to marked diminution of mobility of the lung in these locations is responsible for the prevalence and progression of tuberculosis in these locations.

McMichael and McGibbon in 1944 demonstrated that normal individuals in the recumbent position have a diminished vital capacity and total capacity, but an increase in complemental air. Only recently, Wright et al. showed that in the recumbent position, pneumoperitoneum reduced the total volume and the residual air

in tuberculous patients, but had only a slight effect on the complemental air. However, in a patient who had a phrenic paralysis on one side, in addition to pneumoperitoneum, the most marked change occurred in the complemental air which was greatly reduced. It may be concluded that since complemental air is a measure of the expansibility of the lung, the apices of the lobes share in this expansibility to a greater extent when the unparalyzed diaphragm is functioning in an elevated position.

Trimble et al. in recent years have used phrenic nerve paralysis in only 10 per cent of their cases and "then only for specific and rather narrow indications." One of the largest series of patients treated with both pneumoperitoneum and phrenic nerve paralysis has been reported by Moyer, Veterans Administration Hospital, Oteen, North Carolina. Although his series is much larger than our own, it would appear that the overall percentage results are not greatly different in the two series. Banyai and others have stated that the combination of phrenic nerve paralysis and pneumoperitoneum is superior to either procedure alone because of the fact that the diaphragm can be pushed to a higher level in such cases. In the absence of a functioning diaphragm, it may be necessary to push it higher in order to obtain the desired relaxation to effect adequate drainage. It is believed, however, that when the diaphragm is functioning, its optimum level in pneumoperitoneum is that level which permits of absolute ease of expectoration. In this series of cases, this has been found to vary with the individual patient. Our findings should in no way be interpreted to mean that the combination of pneumoperitoneum and phrenic nerve interruption should not be used. On the other hand, it should indicate that this combination as a routine may not be necessary or warranted.

Streptomycin like pneumoperitoneum has its best results in early exudative cases before irreparable pathological changes have taken place in the lung. It has been observed on numerous occasions that young individuals with fresh pneumonic tuberculosis respond unusually well to streptomycin therapy alone. Some of these patients in fact go on to complete clearing of the pathological process. There is evidence to show that streptomycin, through its suppressant action on the tubercle bacillus, retards the formation of exudates. In the individual with fresh pneumonic tuberculosis without fibrotic changes, free drainage usually follows streptomycin therapy and continues unhampered through an unchanged anatomical bronchial tree. Most of these patients who have had difficult expectoration previous to therapy begin to expectorate freely and with ease soon after therapy has been started.

If early and adequate drainage is not brought about in these

cases, however, permanent productive and fibrotic changes take place in the lung just as they do in pulmonary abscess. In such cases, the drainage mechanism is permanently damaged. This fact not only accounts for the less favorable results following streptomycin therapy in these cases, but it is also believed to account for the more frequent recurrences of active disease. It has been generally accepted that streptomycin therapy in conjunction with collapse therapy in this type of case is the treatment of choice. After studying clinically large numbers of pneumoperitoneum patients in recent years, it has become increasingly clear that the ease of expectoration or the free drainage that occurs following the induction of therapy is the secret to the clearing of the pathological process. One can not but be impressed by the fact that rarely does bronchogenic spread occur when free and adequate drainage exist. This is in contradistinction to the usual spread of disease when a tuberculous endobronchial lesion causes a partial blockage of the bronchus.

The Medical Research Statistics Division, Department of Medicine and Surgery of the Veterans Administration has compiled some interesting figures on tuberculous patients receiving streptomycin alone and also in conjunction with collapse therapy. At the end of 120 days following the institution of a 42 days course of streptomycin in patients showing progressive disease, a bronchopneumonic component and cavity formation, a comparison is made between the two groups. There was a significant increase in the percentage of x-ray clearings, sputum conversion, and reduction of temperature to normal in those patients who received combined therapy as compared to those who had streptomycin alone. In addition, fewer had recurrence of disease in the combined therapy group. In another group of patients with similar pathological changes, except for the presence of cavity formation, combined therapy produced still more favorable results than did streptomycin therapy alone. These findings support our view that the sooner collapse is accomplished before cavity and advanced irreparable pathological changes occur in the lung, the more adequate will be the drainage and the more favorable will be the end results.

Case Material

The therapy conference which includes a thoracic surgeon, formulates an over all plan for the patient when streptomycin therapy is considered. The question of the emergence of resistance of the tubercle bacillus to streptomycin is always kept in mind, and for this reason, streptomycin therapy is coordinated with collapse measures which may also be indicated.

Streptomycin treatment alone may be considered if the patient appears to have a fresh exudative tuberculosis of moderate extent. A plan for collapse therapy, however, may be put into effect at a later date if clearing of the pathological process is not adequate.

Pneumoperitoneum alone may be recommended in patients with or without cavity formation who have a small exudative component. A few of these patients may need major surgery later, but this type of disease usually responds favorably to pneumoperitoneum alone.

Pneumoperitoneum combined with streptomycin therapy is the treatment of choice in patients with bilateral disease who have already developed fibrotic changes, a cavity, and a moderate to marked exudative component. Many of these patients come to major surgery, but gratifying results may be expected without further surgical intervention. Some of them may be converted into "good chronics" even though they may not be suitable surgical risks.

Since the tuberculosis unit at this hospital was activated two years ago, artificial pneumoperitoneum has been induced in 117 patients. Eleven or 10 per cent of them were discontinued because of ineffectiveness of the treatment, or because of irregular discharge and loss of the case to study (Table I). All 11 of these patients at the time of discontinuation of the relaxation therapy had open cavity and positive sputum, but 60 per cent of them had shown some improvement roentgenologically. Seven of them had been given streptomycin in conjunction with pneumoperitoneum. The average length of treatment with pneumoperitoneum in this group of cases was 2.2 months.

Twenty far-advanced patients, 11 of whom are white and nine Negro, have been prepared for major surgery (Table I). None of these had converted his sputum to negative at the time major surgery was decided upon, and all but one had open cavities. All, however, had some clearing roentgenologically. Thirteen received streptomycin in addition to pneumoperitoneum. These were far-

TABLE I

Patients Treated with Pneumoperitoneum and Streptomycin, and With Pneumoperitoneum Alone.

Treatment Status	Number of Patients	Under Active Treatment	Discontinued	for Surgery
PNP and SM	65	45	7	13
PNP Alone	52	41	4	7
TOTAL	117	86	11	20

advanced cases with bilateral disease, and with an exudative component which precluded the use of pneumothorax or any form of major surgery. Without this combined therapy, it is extremely doubtful whether any of these patients could have been salvaged.

Eighty-six patients are at present being treated with artificial pneumoperitoneum. In Tables II and III they are classified as to race, extent of disease, length of treatment and as to whether streptomycin had been given or not. Therapeutic results in reference to cavity closure and sputum conversion are also recorded. It would appear that length of treatment with pneumoperitoneum is an important factor, particularly in the far-advanced cases in determining percentage of cavity closures and sputum conversions, whether streptomycin was administered or not. Of those far-

TABLE II

Length of Therapy	No. of Patients	Cavities Open	Cavities Closed	Sputum Converted	X-ray Improvement
Far Advanced White PNP and SM Patients					
1 - 6 Months	11	7	3	3	7
Far Advanced Negro PNP and SM Patients					
1 - 6 Months	3	2	1	1	2
Total	14	9 (70%)	4 (30%)	4 (29%)	9 (64%)
Far Advanced White PNP Patients					
1 - 6 Months	9	6	2	3	5
Far Advanced Negro PNP Patients					
1 - 6 Months	4	2	1	2	3
Total	13	8 (73%)	3 (27%)	5 (38%)	8 (61%)
Grand Total	27	17 (70%)	7 (30%)	9 (33%)	17 (63%)
Far Advanced White PNP and SM Patients					
6-24 Months	11	4	5	7	10
Far Advanced Negro PNP and SM Patients					
6-24 Months	7	2	5	4	6
Total	18	6 (38%)	10 (62%)	11 (61%)	16 (88%)
Far Advanced White PNP Patients					
6-24 Months	8	2	5	6	7
Far Advanced Negro PNP Patients					
6-24 Months	2	0	2	2	2
Total	10	2 (33%)	7 (77%)	8 (80%)	9 (90%)
Grand Total	28	8 (32%)	17 (68%)	19 (68%)	25 (88.5%)

advanced cases which had been treated less than six months, or an average of 3.3 months, approximately one-third had closed their cavities and converted their sputum to negative. On the other hand, those far-advanced cases which had been treated from six to 24 months, or an average of 11 months, 68 per cent closed their cavities and converted their sputum to negative. When these patients are subdivided into those who had streptomycin therapy in addition to pneumoperitoneum and those who had pneumoperitoneum alone, significant differences are noted, particularly in the groups treated from six to 24 months. In this group, those patients who received pneumoperitoneum alone appear to have done better than those who had been given streptomycin combined with pneumoperitoneum. Of the former group 77 per

TABLE III

Length of Therapy	No. of Patients	Cavities Open	Cavities Closed	Sputum Converted	X-ray Improvement
Moderately Advanced White PNP and SM Patients					
1 - 6 Months	5	2	1	3	4
Moderately Advanced Negro PNP and SM Patients					
1 - 6 Months	2	0	1	2	2
Total	7	2	2 (50%)	5 (71%)	6 (85%)
Moderately Advanced White PNP Patients					
1 - 6 Months	10	1	4	9	9
Moderately Advanced Negro PNP Patients					
1 - 6 Months	1	0	0	0	1
Total	11	1	4 (75%)	9 (82%)	10 (91%)
Grand Total	18	3	6 (66%)	14 (77%)	16 (88%)
Moderately Advanced White PNP and SM Patients					
6-24 Months	5	0	2	4	5
Moderately Advanced Negro PNP and SM Patients					
6-24 Months	1	0	1	0	1
Total	6	0	3 (100%)	4 (66%)	6 (100%)
Moderately Advanced White PNP Patients					
6-24 Months	6	0	4	6	6
Moderately Advanced Negro PNP Patients					
6-24 Months	1	0	0	1	1
Total	7	0	4 (100%)	7 (100%)	7 (100%)
Grand Total	13	0	7 (100%)	11 (85%)	13 (100%)

cent closed their cavities and 80 per cent converted their sputum to negative, whereas in the combined therapy group 62 per cent closed their cavities and 61 per cent converted to negative. These findings undoubtedly reflect the seriousness of the disease at the time therapy was started. Practically all of the streptomycin cases had a moderate to marked exudative component in addition to fibrotic and cavitary disease. Whereas some of the non-streptomycin cases had some degree of exudation at the time pneumoperitoneum was started, it was anticipated that favorable results would be obtained with pneumoperitoneum alone. It might be concluded, therefore, that although length of treatment with pneumoperitoneum is important in determining the eventual outcome of the case, the extent and character of the disease at the beginning of treatment are the deciding factors. This is also exemplified in the 20 patients who were prepared for surgery. Where irreparable changes are so extensive, drainage by means of pneumoperitoneum with or without streptomycin may not be adequate. However, if the disease is not too far advanced and if irreparable changes in the lungs are not too extensive, the institution of drainage may be successful in the great majority of cases. Whereas one-third of the far-advanced cases treated for less than six months closed their cavities and converted their sputum to negative, two-thirds of the moderately advanced cases treated over the same period of time closed their cavities and 77 per cent converted to negative. Of the moderately advanced cases treated from six to 24 months all which had cavities closed them and 85 per cent converted to negative. This compares with 68 per cent closure and conversion of sputum to negative in the far-advanced cases treated over the same period of time. It is recommended, however, that pneumoperitoneum be continued for at least six months before abandonment is considered. It is unusual that spread of disease occurs during the course of pneumoperitoneum therapy, and even though treatment is not in itself successful in some cases in closing cavities and converting sputum to negative, it alone or in combination with streptomycin may be a means of preparing the patient for major surgery.

Thoracoplasty may be successful when other less effective collapse procedures are not, for the reason that it can effectively drain the disease process through adequate collapse. Again recurrence of disease following successful thoracoplasty does not occur for the same reason that the disease process is properly collapsed. Drainage continues unhampered, although this may be slight in amount, until healing occurs and there can be no retrograde spread or retention of exudates as might be the case if the collapse were not adequate. On occasion, however, cavities of the

tension type or others fail to close following thoracoplasty. Successful drainage and eventual healing may be attained in such residual cavities in the use of the Eloesser type of cavernostomy. Reference is made to a previous article in which dramatic relief of acute symptoms followed open cavernostomy in a patient who has since recovered even though he had a high degree of resistance to streptomycin.

The role of drainage in the successful treatment of extrapulmonary tuberculosis is exemplified in the surgical drainage of cutaneous tuberculous sinuses combined with streptomycin therapy. This is described in the original article by the author on this subject.

It has also been observed that tuberculous lesions which occur on the tongue or in canalicular organs, such as the larynx, the bronchi and the intestines heal readily under streptomycin therapy. On the other hand, lesions in organs such as the brain or kidney do not respond as well because of the absence of the free drainage facilities which exist on surface areas.

SUMMARY

An analysis is made of the results obtained in the treatment of 117 patients with streptomycin and pneumoperitoneum combined and with pneumoperitoneum alone. None of them was subjected to surgical paralysis of the phrenic nerve.

The damage to the drainage mechanism of the lungs and bronchial tree following the development within the lungs of irreparable pathological changes and the role of streptomycin and pneumoperitoneum in the restoration of this drainage mechanism are discussed. The sooner collapse by means of pneumoperitoneum is accomplished before cavity and advanced irreparable pathological changes develop in the lung, the more adequate will be the end results.

Length of treatment with pneumoperitoneum is important in determining the eventual outcome of the case, but the extent and character of the disease at the beginning of treatment are the deciding factors in determining this.

RESUMEN

Se analizan los resultados obtenidos en el tratamiento de 117 pacientes con estreptomicina y neumoperitoneo combinados y con neumoperitoneo solo. No se sometió ningún paciente a la parálisis quirúrgica del nervio frénico.

Se discute el daño al mecanismo de canalización de los pulmones y del árbol bronquial subsiguiente al desarrollo dentro de los pulmones de alteraciones patológicas irreparables y del papel que

desempeña la estreptomicina y el neumoperitoneo en el restablecimiento de este mecanismo de canalización. Mientras más pronto se obtenga el colapso con el neumoperitoneo, antes de que se desarrollen cavernas y avanzadas e irreparables alteraciones patológicas, lo mejor serán los resultados finales.

La duración del tratamiento con neumoperitoneo es importante en determinar el desenlace del caso, pero la extensión y el carácter de la enfermedad al principio del tratamiento son los factores decisivos que determinan esto.

RESUME

L'auteur étudie les résultats obtenus chez 117 malades traités par la streptomycine et le pneumopéritoine associés d'une part, et d'autre part le pneumopéritoine seul. La paralysie chirurgivale du nerf phrénique ne fut pratiquée chez aucun d'entre eux.

L'auteur discute les perturbations apportées au drainage du poumon et de l'arbre bronchique par le développement de lésions anatomiques, irréparables, et le rôle de la streptomycine et du pneumopéritoine dans le rétablissement de ce drainage.

Plus le collapsus, grâce au pneumopéritoine, est accompli tôt avant l'apparition de la cavité et le développement des lésions anatomiques avancées, plus le résultat final aura de chances d'être favorable.

La durée du traitement par le pneumopéritoine doit être déterminée par l'évolution de la maladie, mais son étendue et ses caractères lors du début du traitement sont des facteurs capitaux dans cette détermination.

REFERENCES

Banyai, A. L.: Personal communication.

Banyai, A. L.: "Pneumoperitoneum Treatment," *The C. V. Mosby Co.*, St. Louis, 1946.

Brock, Benjamin L. and Woodson, T. Ashby: "Postural Treatment of Pulmonary Tuberculosis," *Ky. Med. Jour.*, (Aug.) 1938.

Brock, Benjamin L. and Woodson, T. Ashby: "Elevation of the Foot of the Bed in the Treatment of Pulmonary Tuberculosis," *Am. Acad. Tuberc. Phys.*, (Aug.) 1939.

Brock, Benjamin L.: "Pathogenesis and Localization of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 42:755, 1940.

Brock, Benjamin L.: "The Role of the Bronchial Tree in the Pathogenesis of Pulmonary Tuberculosis," *Dis. of Chest*, 10:123, 1944.

Brock, Benjamin L.: Discussion of Paper by Bobrowitz, I. D.: "Treatment of Tension Cavities with Pneumothorax," *Dis. of Chest*, 13:133, 1947.

Brock, Benjamin L.: "The Role of the Bronchial Tree in the Pathogenesis of Pulmonary Tuberculosis." Fundamentals of Tuberculosis and Its Complications. *Charles C. Thomas, Publishers*, 1949.

Brock, Benjamin L.: "Streptomycin in the Treatment of Draining Tuberculous Sinuses," *J.A.M.A.*, 135:147, 1947.

Brock, Benjamin L.: "Drainage, Streptomycin, and Tuberculosis," *Dis. of Chest*," 16:129, 1949.

Joannides, M. and Schlack, O. C.: "Use of Phrenic Neurectomy Combined with Artificial Pneumoperitoneum for Collapse of Adherent Lung," *J. Thoracic Surg.*, 6:218, 1936.

Macklin, C. C.: "The Dynamic Bronchial Tree," *Am. Rev. Tuberc.*, 25:393, 1932.
McMichael and McGibbon: Quoted by J. B. Amberson. *Year Book of General Medicine*, 1944.
Medlar, E. M.: "The Pathogenesis of Minimal Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 58:583, 1948.
Medical Research Statistics Division, Veterans Administration: "A Statistical Study of Streptomycin in the Treatment of Pulmonary Tuberculosis." October 21, 1949.
Mitchell, R. S., Hiatt, J. S., McCain, P. P., Easom, H. F. and Thomas, C. D.: "Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 55:306, 1947.
Moyer, Ralph E.: "Pneumoperitoneum and Phreniclasia in the Treatment of Pulmonary Tuberculosis," *Dis. of Chest*, 15:43, 1949.
Murphy, J. D., Elrod, P. D., Walkup, H. E. and Koontz, E. R.: "Surgical Treatment of Residual Cavities Following Thoracoplasties for Tuberculosis," *Dis. of Chest*, 14:694, 1948.
Parnall, C. Jr., Brock, Benjamin L. and Moyer, Ralph E.: "Streptomycin in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, 56: 565, 1947.
Streptomycin Committee, Veterans Administration; Report to the Council on Pharmacy and Chemistry: "Streptomycin in the Treatment of Tuberculosis," *J.A.M.A.*, 138:584, 1948.
Streptomycin Committee, Veterans Administration; Report to the Council on Pharmacy and Chemistry: "Current Status of the Chemotherapy of Tuberculosis in Man," *J.A.M.A.*, 142:650, 1950.
Trimble, Harold G., Eaton, J. L., Crenshaw, G. L. and Gourley, Ina: "Pneumoperitoneum in the Treatment of Pulmonary Tuberculosis," *Am. Rev. Tuberc.*, (May) 1948.
Wright, George W., Place, Ronald and Princi, Frank: "The Physiological Effects of Pneumoperitoneum Upon the Respiratory Apparatus," *Am. Rev. Tuberc.*, 60:706, 1949.

Discussion

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I wish to congratulate Dr. Brock on the excellent presentation of this very interesting and comprehensive paper. Those of us who have been following Dr. Brock's extensive clinical studies fully appreciate the value of his contributions to our knowledge concerning the healing mechanism of pulmonary tuberculosis. His thesis that adequate drainage of the tuberculous areas of the lung is a prerequisite of healing is axiomatic today.

There are certain points in his presentation which deserve particular attention. To do or not to do phrenic nerve operation in combination with artificial pneumoperitoneum is not a simple problem. It is contrary to sound clinical practice to adhere to a single, preconceived dogmatic policy in this respect. Decision as to preference of this combination treatment should be predicated on the type and extent of the disease. It is recognized that the consensus of interested physicians is in favor of using pneumoperitoneum alone in more or less evenly distributed bilateral tuberculous involvement. Of course, it is well known that in unilateral

tuberculosis, favorable therapeutic results often follow artificial pneumoperitoneum without phrenic nerve operation. This is usually the case in tuberculous lesions without widespread bronchopneumonic or pneumonic consolidation. In these instances, there is a free play of the innate centripetal retractility of the involved segments of the lung. This centripetal retractility is enhanced by the decreased pH of the diseased tissues. This phenomenon is commonly defined as selective pulmonary relaxation. Through the same factors, the lung is conditioned for the closure of tuberculous cavities, provided, obvious physical circumstances within the lung itself do not prevent it. I am referring here in particular, to thick fibrosis of cavity walls and to a check-valve mechanism of the draining bronchus of the cavity.

The abstention from phrenic nerve operation, whenever reasonable, is a good practice. It is well to recall in this connection that one hemidiaphragm is responsible for 35 per cent of the function of the corresponding lung. Although it is realized that a diseased lung is not—as a rule—a normally functioning organ, it is referable not to jeojardize potential lung function unless it is absolutely necessary. Also, it is known that in a certain number of instances, temporary phrenic nerve operation carries the risk of losing the function of the corresponding diaphragm permanently.

The situation is, however, entirely different in patients with pronounced degrees of exudative tuberculosis of the lung parenchyma. In such instances, not infrequently, there is a mechanical interference with the physiologic retractility of the diseased regions of the lung. It is obvious, therefore, that if adequate relaxation is the key to the healing of the tuberculous process, it should be attained in such cases by using phrenic nerve operation as an adjunct measure to pneumoperitoneum. There is no need to worry about the occurrence of sudden collapse of the lung when phrenic nerve operation is done after pneumoperitoneum is well established.

Twenty years have elapsed since I introduced artificial pneumoperitoneum in the treatment of pulmonary tuberculosis. It is gratifying to find that today, this method has gained general acceptance all over the world as a useful measure in the management of well selected cases.

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I am presenting the findings in 63 pneumoperitoneum and streptomycin treated cases which have been followed for 12 months or longer. Forty-three per cent were moderately advanced and 57 per cent far-advanced, all were cavitary.

Based on the findings in these cases I recommend that pneumoperitoneum be continued even if the early results are not impressive.

In our series only 8 per cent of the cases closed cavities in three months and 27 per cent in six months, but by the end of 12 months 60 per cent showed cavity closure and after 18 months 70 per cent were closed. Similarly whereas 38 per cent had converted the sputum in six months, this figure was increased to 51 per cent in 12 months and 62 per cent in 18 months (38 per cent did not convert). We used associated phrenic paralysis in only 11 per cent of the cases but are impressed with the relationship between good elevation of the diaphragm and satisfactory clinical and roentgenological results.

We feel that streptomycin and pneumoperitoneum is a good treatment for selected cases of pulmonary tuberculosis and that pneumoperitoneum should be continued over a long period of time.

I am appreciative of Dr. Brocks presentation and also of Dr. Banyai's discussion.

Early Major Surgery After Streptomycin In the Treatment of Acute Pulmonary Tuberculosis*

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Acute pulmonary tuberculosis has always presented a problem in management of seriously ill patients. Before the use of streptomycin the usual treatment consisted of a long period of bed rest in the hope that toxicity would subside and the lesions would be stabilized. Early mortality was always high, approximating 80 per cent. In the surviving cases the clinical course has been long drawn out and with a residual of considerable fibro-caseous cavitary disease. The length of time required before stabilization of the lesion with disappearance of the toxic symptoms was frequently nearly two years, and seldom less than one year. When this stage of chronicity in the disease had been reached the patient was considered ready for major surgery. Other methods of treatment during the acute phase of the disease, such as early pneumothorax or early thoracoplasty, have given unsatisfactory results.[1,2] Pneumoperitoneum also has not been markedly successful.[3] Before streptomycin all forms of therapy used during the acute phase of the pneumonic tuberculosis have left much to be desired.

With the introduction of streptomycin we have received an opportunity for another try at controlling this most serious form of pulmonary tuberculosis. Unfortunately, most of our patients come to us more than a month after the onset of such an acute illness. The golden opportunity for treatment within the first two weeks, before the establishment of caseation, has generally been lost. It has been our experience that most of these patients will show rather prompt decrease of cough, expectoration and general toxicity. They will have a rather slow improvement radiologically and likewise will show a delayed fall of temperature. One factor in delaying admission and treatment of cases of acute tuberculous

*Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration. Read before the Texas Tuberculosis Association, Austin, April 7, 1950. Photographs by Manual Training Division, Veterans Administration Hospital, Kerrville, Texas. (Courtesy M. Fred Faucett).

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pneumonia is the frequent incorrect diagnosis as non-tuberculous pneumonia, with ineffective treatment for a period up to two or more weeks. If treatment with streptomycin could be started promptly, improvement should be much more rapid.

The pathologic process takes much the same course as was seen in pre-streptomycin days but the acute phase is about one-fourth as long with present treatment. Whether the length of time for radiologic and clinical improvement is shorter or longer, the early result of treatment is a sub-acute caseous pneumonic pulmonary lesion, usually with cavitation. Further progress has then been with some degree of fibrosis, partial atelectasis, and the development of chronicity. The difference between pre-streptomycin days and the present then, lies in the length of the period required for stabilization of the acute lesions.

At this time the case is somewhat analagous to that of chronic pulmonary tuberculosis with recent spread, perhaps from open cavity with or without hemorrhage, which has been treated with streptomycin. Improvement has been observed radiologically in about 70 per cent of such patients.[4] Unfortunately, follow-up of these patients has shown relapse or recurrence of disease in 25 per cent of those improved, during the first year following streptomycin and by the end of the second year some 40 per cent of those previously improved under treatment have relapsed. Moyer,[5] at Oteen, treated 37 cases of massive tuberculous pneumonia with streptomycin, followed by pneumoperitoneum in 27, with maximum clearing of the pulmonary lesion in 16, moderate clearing in 12, and sputum conversion in 22. Late reports are not available to us to determine the rate of relapse in the cases improved under this treatment.

Kirby, Simpson and Creger[6] report relapse after improvement in 11 of 15 adult Negroes treated with streptomycin for acute tuberculous pneumonia, without surgery; they consider properly timed adequate surgical collapse essential for permanent improvement. Obviously, the persistently open disease process has not been controlled more than temporarily, by antibiotics alone. Something more has been required to consolidate the improvement, and to prevent the late relapses and late spreads of disease that have nullified the effect of good medical treatment. In an attempt to hold the gains, and to approach the end-result of arrested disease, we adopted the policy of offering surgical therapy to such patients, when the disease process had been brought under control, as evidenced by disappearance of general toxicity, and by radiologic evidence of stabilization of the lesion or (presumably) maximum early improvement. In none of these patients with acute caseous-pneumonic pulmonary tuberculosis have we seen complete clearing,

or "healing" of the lesions under streptomycin and medical treatment. Recently it has been our policy not to await complete clearing or complete stabilization of disease in our patients treated for massive tuberculous pneumonia or other acute caseous pneumonic tuberculosis. Instead, we are inclined to apply permanent (surgical) collapse or other major surgical procedure as soon as we believe that the disease is under control, or that the immediate maximum of improvement has occurred. Early thoracoplasty has been used at Fitzsimons General Hospital[7] in the management of such cases. Their report includes 12 cases, all of whom had surgical collapse measures instituted from four to 12 months following acute onset of disease, with satisfactory results. (Eight of 12 had sputum conversion, as of December 1948, from four to 15 months post-operatively).

Treatment in such cases must be individualized. We believe, from the course of the disease in the eight cases described, that early major surgery following treatment with streptomycin offers the best prognosis for the patient with acute spread of disease, with or without hemorrhage. We believe, also, that delay is needless and dangerous in such cases, because of the danger of relapse of these insufficiently stabilized lesions.

We are reporting eight cases subjected to major surgery after treatment for acute tuberculous pulmonary disease. Of these, six had onset with acute pneumonic disease and were admitted to this hospital acutely ill with moderately high fever and extensive confluent disease of broncho-pneumonic distribution and one had a large tension cavity in the left upper lobe with recent increase of disease, following influenzal respiratory infection. Treatment with streptomycin was given and permanent surgical collapse measures instituted as soon as it was thought that maximum improvement had been secured, or that stabilization had occurred. Six cases received thoracoplasty. One case was treated with extrapleural plombage and one with total pneumonectomy. First stage of thoracoplasty was done from one and one half to five months, the extrapleural plombage three months and the pneumonectomy two weeks after beginning of streptomycin treatment. At present, with follow-up from seven to 32 months post-operative, seven of these eight have negative sputum, and all are in good condition.

The exact surgical procedure to be employed is not the issue at this time. We feel it is most important that advantage be taken of the stabilizing and bacteriostatic effect of antibiotic therapy, and that at the proper time in each case, when early improvement shall be judged to have reached its maximum, adequate surgical treatment should be employed. Thus we may secure stabilization of the disease, and only in this way can we avoid the relapses and

recurrences of disease, that may at any moment place the patient beyond the help of any method of treatment whatever.

A.C.: This 25 year old Latin American Veteran had onset about a month before admission (August 17, 1946) with pain in the chest and between the shoulders, fever, productive cough and slight weight loss. He had also had anorexia and weakness for about two weeks. Temperature on admission was 103 degrees F., he was sweaty, weak and toxic. By physical examination including x-ray inspection he had evidence of involvement of the entire left lung with positive sputum. X-ray film showed a completely cloudy left chest with suggestions of multiple cavitation, and a slight fibrotic infiltration in the right second anterior interspace.

On bed rest over a period of three months he remained acutely ill. His temperature declined but still reached 100 degrees F. daily. His expectoration varied from three to six ounces of thick muco-purulent sputum daily and there appeared deviation of the trachea and mediastinum toward the left, suggesting either atelectasis or broncho-stenosis of high grade. Bronchoscopic examination December 18, 1946 revealed only inflamed left lower lobe bronchial mucosa. Sputum remained persistently positive. A bronchogram revealed saccular dilatations throughout the left upper lobe and streptomycin was begun on January 31, 1947, preparatory to surgical excision of the left lung.

Weight was 101 pounds, temperature was about 102 degrees F. when left pneumonectomy was done February 14, 1947. The specimen showed total destruction of the left lung with caseous pneumonic tuberculosis.



FIGURE 1: August 21, 1946. Admission Film. Onset of acute pneumonic disease 1 month before admission. Small contralateral infiltration indicated by arrow.

TABLE I: SUMMARY OF TREATMENT AND RESULTS

CASE	TIME FROM Onset to — — Surgery — —	TIME FROM SM O-day to — — Surgery — —	Operation	Post-operation Period	Complications	Present Condition Clin.	Present Condition Bact.	REMARKS
WEF	13 mo.	5 mo.	THplsty.	9 mo.	none	VG	neg. (G)	Contralat. Pnx. Tuberc. Larynx healed
JA	7 mo.	1½ mo.	THplsty.	13 mo.	none	VG	neg. (G)	
HCW	7 mo.	5 mo.	THplsty.	7 mo.	none	VG	neg.	
SS	4½ mo.	4 mo.	THplsty.	10½ mo.	Atelect. RLL between stages	VG	neg. (G)	
FA	4 mo.	3 mo.	ExtrPl.	8½ mo.	Pleural effus. at 5 mo. post-op. on oper. side	G	neg. (G)	Pleural effusion, cul. pos. AFB, now cleared.
CG	3 mo.	7 wks.	THplsty.	8½ mo.	none	G	pos. (G)	24 hr. conc. sptum. neg. gastric cul. running.
JB	2 mo.	5 wks.	THplsty.	11½ mo.	none	G	neg.	AWOL 6½ mo. post-op.
AC	5 mo.	2 wks.	PNectomy.	32 mo.	Spread post-op.	VG	neg.	Recurrent contralat. infiltr. at 16 mos. without symptoms. Now markedly improved.

LEGEND: THplsty.: Thoracoplasty.
ExtrPl.: Extrapleural pneumonolysis with lucite ball plombage.
Pnx.: Pneumothorax.
Condition: Clin.: G, Good; VG, Very good.
Bact.: G, Gastric content (culture); Unspecified: 24 hr. sputum concentrate, culture.

Following operation a spread appeared throughout the right lung and streptomycin was continued until April 9, 1947, a total of 70 days and 140 grams of streptomycin. It was discontinued when the patient's white cell count dropped to 6000 with 53 per cent polys which was considered a dangerous leukopenia. After a slight further drop, white count and polymorphs percentage increased and recovery thereafter was uneventful. The spread in the right lung cleared. The patient's condition improved markedly immediately following the operation. He gained 10 pounds of weight within the first two weeks and maintained a continuous improvement thereafter. His sputum following operation was consistently negative and on May 7, 1947 he weighed 120 pounds.

In August 1948, 16 months post-operatively, there was x-ray evidence of a recurrence of disease in the right anterior second interspace but he was asymptomatic. He was re-admitted to the hospital. On bed rest this man has improved and his sputum has remained negative. He is now in good condition with negative sputum (including gastric cultures). He is 32 months post-operative. Concentrates were negative October 24, 1949 and cultures were started.

W.E.F.: A 20-year old white male had intermittent pleural pain in October 1947. He had cough productive of about one half ounce of sputum, night sweats and loss of 30 pounds weight in four months, sore throat for approximately a month before admission (July 11, 1948) and a hemoptysis that persisted for about a week in the month preceding admission to this hospital. His sore throat had been treated with penicillin without improvement and when admitted he ran a low grade fever up to 100 degrees F.

Examination revealed bilateral upper lobe infiltration with a moderately large cavity in the left upper lobe below which appeared a fairly fresh spread of disease of an apparently caseous pneumonic character. In addition to bed rest care, pneumothorax, right, was initiated July 21, 1948 and streptomycin 1 gram, for 42 days beginning July 27, 1948 was

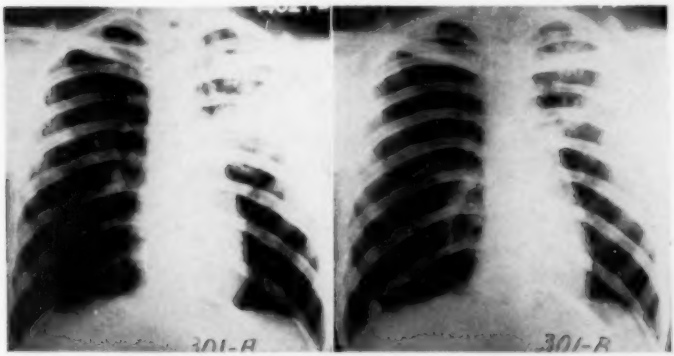


FIGURE 2a FIGURE 2b

Fig. 2a: July 14, 1948. Admission film. Ten months after onset and 3 weeks after hemoptysis; acute illness with spread.—*Fig. 2b:* December 15, 1948. Three months after 42 gms. SM. First stage 8 days later. Discharged—Arrested 15 months later.

given for tuberculosis of the larynx. The laryngeal disease improved rapidly and the right pneumothorax was satisfactory.

A two-stage, seven-rib thoracoplasty, the first stage on December 23, 1948, 150 days after beginning of streptomycin was completed January 2, 1949. This patient has gained weight, all sputum examinations since operation have been negative, and he is in good general condition. His pneumothorax is being continued and he is on our convalescent service. Culture of gastric specimens taken in July 1949 have been reported negative. He is now nine months post-operative.



FIGURE 3a



FIGURE 3b

Fig. 3a: July 17, 1948. Outside film 1 month before admission to hospital and 2 weeks after positive sputum and induction of Pnx. right by patient's LMD.—*Fig. 3b:* August 16, 1948. Admission film—acute caseous pneumonic disease under right Pnx. *(Not Atelectasis)*. Bronchoscopy w/aspirations 5 times. Also Br. Pn. extension into RLL Pnp. instituted at end of SM and Thpisty. First stage 3 months later. Discharged arrested 13 months after completion of Thpisy. and 20 months after admission.



FIGURE 4a

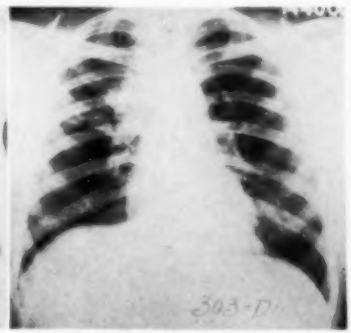


FIGURE 4b

Fig. 4a: Acutely ill 2 weeks with fever. Hemoptysis day before admission. Bedside film—2 months later. Patient acutely ill. SM 42 gms. begun for progressively increasing disease which responded well, leaving residual cavity.—*Fig. 4b:* Four months later and improved before thoracoplasty. Discharged "Arrested" 1 year later—20 months after admission.

J.A.: This Latin American male of 24 years had a "bad chest cold" in February 1948 with fever, cough, sore throat and chest pain. In March he had increased productive cough and hemoptysis and lost about 20 pounds weight. X-ray film of the chest at that time showed pulmonary tuberculosis and he was admitted May 26, 1948 to Brooke General Hospital where streptomycin treatment was begun on June 2. On transfer to this hospital June 17, streptomycin was continued, and he received 1 gram daily for 42 days.

On admission his sputum was positive for tubercle bacilli, and there was x-ray evidence of pneumonic disease involving the entire right upper lobe with some honeycombing and slight infiltration in the left upper lobe. His toxic symptoms subsided and a two-stage, seven-rib thoracoplasty was done. The first stage was 120 days (September 9, 1948) from beginning of streptomycin therapy. The second stage was on September 30, 1948. His post-operative course was entirely uneventful. Sputum examinations including cultures were negative, except for one positive culture on March 15, 1949, and clinically the patient has been in good condition. Culture of gastric washings of August 10, 1949 (10 months post-operative) was reported negative for tubercle bacilli.

H.C.W.: This white male of 26 years, when admitted August 10, 1948 was acutely ill with temperature of 101 degrees F. He had loss of weight and strength for the preceding year or more and productive cough for two months. One month before admission, positive gastric washings were obtained by his physician and right pneumothorax was begun immediately and continued up to admission to this hospital.

A review of his case showed evidence of acute caseous pneumonic tuberculosis in the right upper lobe with broncho-pneumonic extension in the lower half of the lung, for which streptomycin was given, 1 gram daily for 42 days (September 3 to October 27, 1948). The pneumothorax was abandoned and the expanded lung showed marked improvement in the right upper lobe, but with a cavity adjacent to a consolidated apical segment. Because of persistent active infiltration in the right base, pneumoperitoneum was begun November 9, 1948 with improvement in the following three months so that a three-stage, nine-rib thoracoplasty was

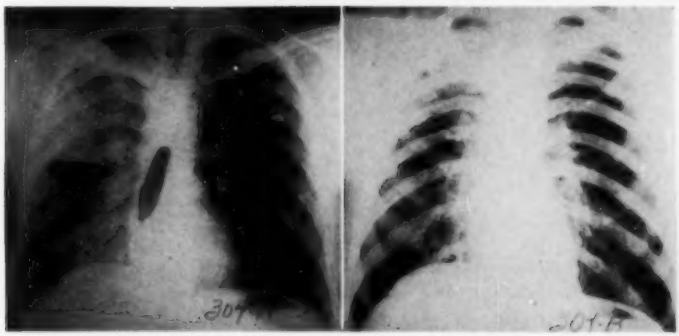


FIGURE 5a FIGURE 5b

Fig. 5a: February 15, 1948. Acute pneumonic infiltration R.U.L. duration 1 month.—*Fig. 5b:* August 2, 1948. After 96 gms. SM—Marked improvement.

performed February 12, 1949, the first stage 191 days after beginning of streptomycin treatment. The second and third stages were done on March 5 and 25, 1949. Post-operative course was uneventful. He promptly gained weight and all sputa have been reported negative. His general condition is good. He is now six months post-operative.

S.G.S.: This Latin-American male of 21 years had fever for two weeks and hemoptysis for one day before admission on April 3, 1948, at which time he was toxic, with temperature of 101 to 102 degrees F. He had evidence of extensive soft infiltration in the right upper lobe, with sputum positive for tubercle bacilli. Pneumothorax, right, was attempted unsuccessfully. Following a pulmonary hemorrhage his temperature ranged from 102 to 104 degrees F. and streptomycin was given, 1 gram daily for 42 days (June 16 to July 27, 1948), for increasing disease. The acute disease process subsided and thoracoplasty, right, was performed, first stage on October 12, 1948, 120 days after beginning streptomycin. The second stage was delayed by a pleural effusion on the operated side requiring aspiration on two occasions. Fever with atelectasis in the right base was relieved by bronchoscopic aspiration of the right middle lobe and the second stage of thoracoplasty was performed December 8, 1948. Marked subcutaneous emphysema developed over the chest, abdomen and acrotum which subsided shortly and his course thereafter was uneventful. Sputum examinations have been negative since the second stage, including cultures and guinea pig of sputum six months post-operatively. His general condition is good; he has been gaining weight and is on increased activity.

F.A.: A Latin-American male of 28 years had acute pneumonic disease in February 1948 and was treated unsuccessfully with sulphonamide or sulfonamide and penicillin, following a one month history of fever, productive cough, and weight loss of 24 pounds. At Brooke General Hospital he was extremely toxic with temperature ranging from 102 to 104 degrees F. and was treated with streptomycin, 1 gram daily for 96 days.

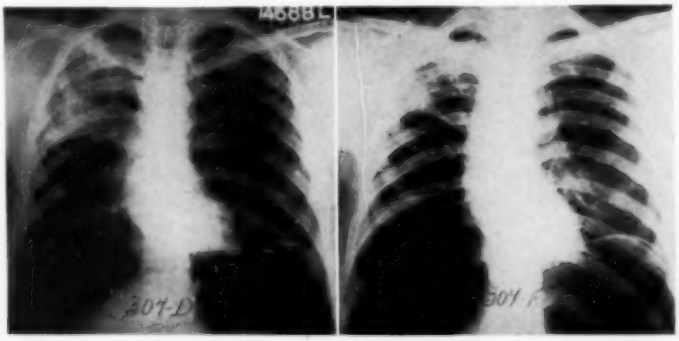


FIGURE 5c FIGURE 5d

Fig. 5c: November 3, 1948. Increased disease in right base after hemorrhage. Residual of Pnx. given for control of hemorrhage present. Pnp. started and SM begun (42 gms.).—*Fig. 5d:* February 2, 1949. Clearing of right base. Pre-operation film.

He was transferred to this hospital on June 15, 1948, where sputum was positive, and he ran a slightly elevated temperature to 99.6 degrees F. The right lung contained an extensive confluent broncho-pneumonic lesion involving the entire right upper lobe with cavity, with disease also in the right base. After six weeks in this hospital he was afebrile.

The right basal spread had improved after four months and thoracoplasty, right, was recommended. On October 15, 1948 there occurred a sudden hemoptysis of three to four ounces, apparently from the right side, which ceased following pneumothorax, right. Increase of disease in the right lung was treated with streptomycin, 1 gram daily for 42 days (November 4 to December 15, 1948), with some clearing and with considerable improvement in temperature, cough and expectoration. The left lung now appeared clear. Because of some diminution of renal function and findings suggestive of amyloid degeneration, one-stage procedure was considered preferable, and on February 5, 1949, three months from the beginning of the second course of streptomycin, this patient had an extrapleural pneumonolysis on the right with lucite ball filling. The post-operative course was satisfactory and he gained 10 pounds soon after surgery.

About the end of June 1949, four and one half months post-operatively, he again began to run temperature up to 101 degrees F. and was found to have a fairly large effusion in the pleural cavity below the extrapleural space. This was aspirated of 1500 cc. of clear fluid, positive for tubercle bacilli on culture. His temperature fell to normal after 10 days and has remained so. There was some evidence of continued active disease in the right base below the extrapleural space. Sputum cultures, however, reverted to negative after March 1949 and have remained so up to six months post-operative. Three cultures (gastrics) about August 8, 1949 were negative. His clinical condition is fairly good but his weight is somewhat low.

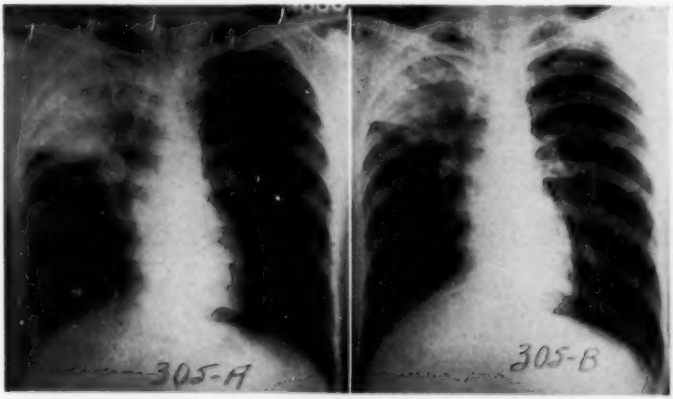


FIGURE 6a FIGURE 6b

Fig. 6a: November 3, 1948. Acute disease, onset 4 months before this film, which shows condition at start of treatment with 0.5/42 SM.—*Fig. 6b:* December 17, 1948. Moderate retraction of disease RUL but little resolution after SM.



FIGURE 7a FIGURE 7b FIGURE 7c

Fig. 7a: June 11, 1948. Small infiltration L.U.L.—*Fig. 7b:* July 20, 1948. Six weeks later—acute spread of disease, left, with high fever. SM 1.0/42 begun.—*Fig. 7c:* September 21, 1948. Showing moderate clearing at close of SM course, which was followed promptly by thoracoplasty next day. Result: Sputum culture negative—patient AWOL 7 months post-operative (completion of thoracoplasty). In good general condition.

C.G.: This Latin-American male of 26 years had fever, weakness and easy fatiguability beginning August 1948, after a weight loss of 20 pounds in the preceding six months. On several occasions during September 1948, he had hemoptysis. Pulmonary tuberculosis was reported from x-ray inspection of chest in September 1948. He complained of pain about the right scapula with occasional nausea and vomiting following severe cough. His temperature was elevated to approximately 101 degrees F. daily on admission (October 25, 1948). A diagnosis was made of acute caseous pneumonic tuberculosis involving the entire right upper lobe and he was treated with bed rest plus streptomycin (0.5 gram daily for 42 days) administered from November 4 to December 15, 1948. Some improvement was noted by x-ray inspection.

A three-stage, seven-rib, right thoracoplasty was begun on December 22, 1948 when it was thought that maximum early improvement and some degree of stabilization had occurred. The first stage was performed on the 49th day following the beginning of treatment with streptomycin. The second and third stages were done on January 10 and February 1, 1949. Sputum concentrate examinations were negative. A culture of sputum on May 11, 1949 was positive with organisms sensitive to 10 mcgm. of streptomycin, and culture of gastric contents taken July 12, 1949 was reported positive. Clinically he is in good condition and he is now eight months post-operative.

J.B.: This white male Veteran of 26 years was a prisoner of war for 42 months in Burma. When liberated in August 1945, he weighed 84 pounds. Following his discharge from the Army with a diagnosis of pulmonary tuberculosis, he was in three different tuberculosis hospitals for periods of a month or less with sputum smears and guinea pig inoculation of sputum reported negative. He was re-admitted to this hospital on April 27, 1948 following x-ray evidence of markedly increased disease but again left A.W.O.L.

On present admission, July 19, 1948, he had elevated temperature to 99.4 degrees F. and left chest pain with physical and x-ray evidence of spread of disease in the left lung. His temperature was irregular and



FIGURE 8a FIGURE 8b

Fig. 8a: June 18, 1948. Admission film—3 weeks of SM begun elsewhere for acute exudative disease RUL—after hemoptysis.—*Fig. 8b:* September 2, 1948. Six weeks after completion of 42 gms. SM. Discharged apparently arrested 10 months later—13 months post-admission.

ranged up to 101 degrees F. Pneumothorax was attempted unsuccessfully. On August 5, 1949 it was observed that there had been rapid spread in the left upper lobe since two months earlier. Sputum had been consistently positive for tubercle bacilli. There was a confluent bronchopneumonic disease process throughout the left upper lobe with excavation and the patient received streptomycin, 1 gram daily for 42 days, ending September 22, 1948. Bronchoscopy showed no endobronchial disease and three-stage, nine-rib thoracoplasty was done, the first stage (September 22, 1948) on the 42nd day following institution of streptomycin therapy. The second and third stages were done October 11 and November 9, 1948. Post-operative course was uneventful. His sputum was negative following surgical collapse, including cultures, except for one positive culture on January 12, 1949, organisms being sensitive to 10 mcgm. of streptomycin. Subsequent sputum cultures were negative. This patient left the hospital A.W.O.L. on May 30, 1949 in good clinical condition when six months post-operative.

SUMMARY

In the past 36 months we have treated eight patients for acute tuberculous pulmonary disease with streptomycin, followed within five months by major surgery. Surgical therapy was employed as early as it was thought that the acute lesions had become stabilized, *or when early maximum improvement was considered to have occurred*. All patients are clinically in good condition. One patient only, at the last report, has had positive cultures of gastric contents.

The time from onset of disease to surgical collapse or excision averages less than six months, and in six of the eight, averages slightly over four months.

Follow-up on these patients now ranges from seven to 32 months post-operatively.

RESUMEN

En los últimos 36 meses hemos tratado ocho casos de tuberculosis pulmonar aguda con estreptomicina seguida después de cinco meses por la cirugía mayor.

La cirugía se empleó tan pronto como se consideró que las lesiones se habían estabilizado o *cuando se consideró que se había obtenido el máximo de mejoría pronta*.

Todos los enfermos están en buenas condiciones clínicamente, solamente un enfermo, según el último informe, ha tenido cultivos positivos de contenido gástrico.

El tiempo desde el principio de la enfermedad hasta el colapso quirúrgico o resección, es por término medio de seis meses y en seis de los ocho, es ligeramente más de cuatro meses.

La observación ulterior de estos enfermos es de 7 a 32 meses después de la operación.

RESUME

Dans les derniers trente six mois, les auteurs ont traité huit malades atteints de tuberculose pulmonaire aigue par la streptomycine puis ils ont fait suivre ce traitement par une grande intervention chirurgicale moins de cinq mois après sa terminaison. Le traitement chirurgical a été utilisé dès que les lésions aigues parurent stabilisées. Il fut également utilisé dès qu'on eut l'impression qu'on était arrivé au point maximum de l'amélioration. Tous les malades sont cliniquement en très bon état. Un seul d'entre eux a eu, à la dernière observation, une culture positive sur tubage gastrique.

Le délai qui s'étend depuis le début de la maladie jusqu' au moment de la collapsothérapie ou de l'éxerese est inférieur à six mois en moyenne; dans bien des cas il ne dépassa pas quatre mois.

Révision des observations de ces malades avec un recul de sept à trente deux mois après l'opération.

REFERENCES

1 Goldberg, B.: "Clinical Tuberculosis," *F. A. Davis Co.*, Philadelphia, 1946. Vol. 1, p. B-110 et seq.
2 Packard, E. N., Hayes, J. N. and Blanchet, S. F.: "Artificial Pneumothorax," *Lea and Febiger*, Philadelphia, 1940, p. 38.
3 Banyai, A. L.: "Pneumoperitoneum Treatment," *C. V. Mosby Co.*, St. Louis, 1946, p. 200.
4 Hinshaw, H. C.: "Comments on Tabular Data," *Minutes of the Sixth Streptomycin Conference*, Veterans Administration, October 1948, p. 12.
5 Moyer, R. E.: "The Treatment of Massive Tuberculous Pneumonia," *Minutes of the Sixth Streptomycin Conference*, Veterans Administration, October 1948, p. 14.
6 Kirby, Wm. M., Simpson, R. M. and Creger, W. P.: "Streptomycin Therapy of Tuberculous Pneumonia in Negro Adults," *Am. Rev. of Tuberc.*, 60:343, 1949.
7 Forsee, J. H. and Erman, E. D.: "Extrapleural Thoracoplasty Performed Early in Caseopneumonic Tuberculosis," *Minutes of the Seventh Streptomycin Conference*, Veterans Administration, April 1949, p. 155.

Streptomycin Para-Aminosalicylate in the Treatment of Pulmonary Tuberculosis*

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In October 1946, leaning upon the experiences of Drs. Hinshaw[1] and McDermott,[2] a group of 20 patients in the Livermore Veterans Hospital, California, who had active progressive pulmonary tuberculosis, were placed on streptomycin therapy according to common protocols mutually agreed upon by the Veterans Administration, Army and Navy.[3] Since then, over 500 patients at the Livermore Veterans Hospital have received some form of anti-microbial therapy for various tuberculous conditions. Many of these patients required more than one course of chemotherapy. In all protocol cases, roentgenograms, laboratory data including streptomycin sensitivity studies, and caloric and audiogram tests were routinely performed during the pre-treatment, treatment, and post-treatment periods.

The primary question as to whether streptomycin was an effective drug was quickly satisfied but a host of subsidiary questions arose.[4] Would larger doses be more effective, or smaller doses less effective? What is the optimum duration of treatment? How can toxic manifestations and the emergence of drug resistant microorganisms be diminished or abolished?

The following 17 treatment regimens have been successively employed at Livermore:

1) 1.8 Gm. Streptomycin a day (0.3 Gm. q 4 h.) for 120 days.
2) 1.0 Gm. Streptomycin a day (0.5 Gm. b.i.d.) for 120 days.
3) 0.5 Gm. Streptomycin a day for 120 days.
4) 0.5 Gm. Streptomycin a day for 42 days.
5) 1.0 Gm. Streptomycin daily and 15 Gm. Para-aminosalicylic acid (0.5 Gm. t.i.d.) for 120 days.

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*Presented at the Sixteenth Annual Meeting of the American College of Chest Physicians, San Francisco, California, June 25, 1950.

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Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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6) 1.0 Gm. Streptomycin and 8 Gm. Promizole daily for 120 days.
7) 1.0 Gm. Streptomycin every fifth day for 42 doses over a 210 day period.
8) Para-aminosalicylic acid (PAS) 3.0 Gm. q.i.d. for 42, 90 and 120 day periods.
9) 2.0 Gm. Dihydrostreptomycin daily for 42 days.
10) 1.0 Gm. Streptomycin and 3.0 Gm. PAS q.i.d. for 90 and 120 day periods.
11) 1.0 Gm. Dihydrostreptomycin and 3 Gm. PAS q.i.d. for 90 and 120 day periods.
12) 1.0 Gm. Streptomycin or Dihydrostreptomycin twice a week and 3 Gm. PAS q.i.d. for 90 days.
13) Same as No. 12 for 120 days.
14) Streptomycin Para-aminosalicylate daily for 90 days.
15) Tibione (TB 1) 100 mgm. b.i.d. for 120 days.
16) Tibione and 1 Gm. Streptomycin for 120 days.
17) Terramycin 7.5 Gm. daily.

From the aforementioned list of regimens it is apparent that methods of suppressing the emergence of resistant strains of tubercle bacilli to streptomycin or dihydrostreptomycin have consisted of short courses, intermittent courses, and combination with other bacteriostatic drugs, e.g. promizole, para-aminosalicylic acid and tibione. Of these various methods, the combination of intermittent streptomycin or dihydrostreptomycin and oral para-aminosalicylic acid appears to be the most effective, so far, in delaying the emergence of streptomycin resistant microorganisms without losing therapeutic efficacy.[5] Studies to date have emphasized the large dosages of PAS (8 to 15 Gm. per day) necessary in order to delay the emergence of resistant microorganisms; and the frequent gastro-intestinal disturbances resulting from the administration of these large doses orally.[6] Dr. Warner has reported that the eight gram daily dosage cases show definitely less tendency to delay resistance than the higher dosage.[7]

The para-aminosalicylic acid salt of streptomycin is a highly purified compound consisting of 56 parts of streptomycin base and 44 parts of PAS. One molecule of pure streptomycin base combined with three molecules of para-aminosalicylic acid to form the water soluble salt, streptomycin para-aminosalicylate; one Gm. of streptomycin combining with 0.8 Gm. PAS. The original observations in animals treated with this salt by Dr. Gladys Hobby[8] indicated that the small amount of PAS present in this molecule is sufficient to exert a synergistic effect with streptomycin and that it is sufficient to lower the dosage of streptomycin necessary to suppress tuberculous infection in experimentally inoculated

mice. It is approximately twice as active in vitro as streptomycin alone when compared on a streptomycin unitage base. In vitro studies to demonstrate the emergence of strains resistant to streptomycin para-aminosalicylate failed to show such mutants during a three-month study. It was recognized that this did not mean that such resistant organisms would not appear under appropriate conditions. The data available suggested, however, that the incidence with which strains resistant to this salt would appear is low.

More recently Karlson[9] at the Mayo Clinic has studied the effect of the dihydrostreptomycin salt of PAS in experimental guinea pig tuberculosis. He concluded that the dihydrostreptomycin salt of PAS was as effective, but not superior to dihydrostreptomycin alone.

Following the preliminary animal experimentation by Dr. Hobby, the study of the PAS salt of streptomycin was undertaken in 1949 by five of the Veterans Administration Hospitals (Sunmount, Newington, Oteen, Chamblee, and Livermore). Dr. McLeod Riggens, Dr. John Adcock[10] and Dr. William Stearns have an additional series of patients under treatment with the salt.

Clinical Material: The salt was administered daily, in a single intramuscular injection over a 90-day period. The tuberculosis in 19 patients was classified as far advanced and in one as moderately advanced. The patients were all males: 14 white, four negro and two Japanese. Ages varied from 21 to 61 years with 10 under 40 and 10 over 40 years. None had received previous streptomycin or PAS therapy.

Response to Treatment

Temperature: In 10 patients the temperature remained normal throughout treatment. In nine it was elevated at start of therapy (over 99.6 degrees) and returned to normal. In one who was quite toxic, the temperature averaged 101 degrees at the start and 99.6 degrees at the end of treatment.

Weight: Five patients gained in excess of 16 pounds; five gained between 11 and 15 pounds; two gained between five and 10 pounds; five gained less than four pounds and two lost 14 and 16 pounds, respectively.

Roentgenograms: Cavitary component was suggestive in seven of the 20 patients. Bilateral disease was present in 17. In no instance did it appear that progression of the disease was not being suppressed when roentgenograms were compared at the beginning and end of treatment. Marked improvement was noted in one; moderate improvement in eight; slight improvement in five; and six appeared unchanged.

Laboratory Data

Sensitivity Tests: Tubercle bacilli obtained from the sputum of each patient just prior to the institution of treatment were inhibited in vitro by less than 1.0 mcg. streptomycin per milliliter of medium. Sensitivity studies after 30 days of treatment in 17 patients showed that the bacilli were still sensitive in all 17. Sensitivity studies after 60 days in 15 patients showed that the bacilli were still sensitive in 14 and resistant in only one patient. At 90 days, studies have been reported in 17 patients, only nine of whom are still sensitive. The remaining eight are resistant in the intermediate zone (10-100). This suggests that the development of resistance in our cases was delayed beyond the 60-day treatment point but not beyond 90 days. In many cases, sputum for culture of tubercle bacilli could only be obtained by resorting to gastric lavage cultures.

Although it is known that resistance to PAS may develop after prolonged PAS therapy, there were no instances of PAS resistance after 90 days' treatment.

Blood Levels: Absorption curves of the PAS portion of the streptomycin para-aminosalicylate indicated peak concentration occurred most frequently one hour after injection.[11] Eighty-three samples obtained at the one-hour interval showed an average of 1.2 mgm. per cent uncombined PAS. Trace amounts were found in the plasma after four hours.

Toxic Manifestations: Untoward reactions were encountered in none of the patients. Apparently, the gastro-intestinal irritation produced by the oral administration of PAS has been circumvented. However, symptoms due to streptomycin were still present. Transient vertigo was noted in five patients, ataxia in one, dermatitis in two, transient casts in one and eosinophilia (over 6) in three. Caloric tests at the end of treatment were normal in each patient. There was no diminution in hearing.

SUMMARY

1) Twenty patients with progressive pulmonary tuberculosis received daily injections of the PAS salt of streptomycin for 90 days.

2) Two anti-microbial agents have been combined for parenteral administration, with a satisfactory therapeutic response. This indicates that a combination of anti-microbial agents which might prove more effective because of synergistic action and a delay in the emergence of resistant microorganisms is a possibility.

3) The rate of development of resistant strains of tubercle bacilli appeared to be delayed beyond the 60-day period of treatment.

4) Resistant strains appeared to develop more rapidly in those

patients whose roentgenograms showed evidence of cavitary disease.

5) Gastro-intestinal irritation due to PAS was circumvented.

RESUMEN

1) Veinte pacientes con tuberculosis pulmonar evolutiva recibieron inyecciones diarias del para-aminosalicilato de estreptomicina por 90 días.

2) Se han combinado dos agentes anti-micróbicos para la administración parenteral, con un resultado terapéutico satisfactorio. Esto indica la posibilidad de que se obtengan combinaciones de agentes antimicróbicos que resulten más eficaces debido a una acción sinérgica y al aplazo en la aparición de microorganismos resistentes.

3) Pareció que no se desarrollaron cepas resistentes de bacilos tuberculosos sino después de 60 días de tratamiento.

4) Pareció que se desarrollaron cepas resistentes con más rapidez en aquellos pacientes cuyos roentgenografías mostraron signos de cavernas.

5) Se evitó la irritación gastrointestinal debida al PAS.

RESUME

1) Vingt malades atteints de tuberculose pulmonaire évolutive ont reçu chaque jour une injection de PAS ou de streptomycine pendant 90 jours.

2) Ces deux produits antimicrobiens ont pu être combinés pour être administrés en injection. Cette thérapeutique a donné des résultats tout à fait satisfaisants. Ceci démontre que la combinaison d'agents antimicrobiens est possible. Elle est accrue par l'action synergique des deux produits, en même temps que la streptomycino-résistance se trouve retardée.

3) Le moment du développement des souches résistantes des bacilles tuberculeux se trouve reporté au-delà d'une période de 60 jours de traitement.

4) Les souches résistantes semblent se développer plus rapidement chez les malades dont la radiographie fait la preuve de cavernes.

5) Les troubles gastro-intestinaux dus au PAS ont été combattus.

REFERENCES

1 Hinshaw, H. C. and Feldman, W. H.: "Streptomycin: A Summary of Clinical and Experimental Observations," *Jour. Pediat.*, 28:269, 1946.

2 McDermott, W.: "Toxicity of Streptomycin," *Amer. Jour. Med.*, 12:491, 1947.

3 "The Effect of Streptomycin Upon Pulmonary Tuberculosis; Preliminary Report of a Cooperative Study of 223 Patients by the Army, Navy and Veterans Administration," Prepared by the Streptomycin Committee, Veterans Administration, Washington, D. C., *Am. Rev. Tuberc.*, 56:485, 1947.

4 Walker, A. M. and Barnwell, John B.: "Clinical Evaluation of Chemotherapeutic Drugs in Tuberculosis," *Annals of N. Y. Acad. of Sc.*, 52: 742, 1949.
5 Minutes of Ninth Streptomycin Conference, April 1950, St. Louis, Mo.
6 Dunner, E., Brown, W. B. and Wallace, J. L.: "The Effect of Streptomycin with Para-aminosalicylic Acid on the Emergence of Resistant Strains of Tubercle Bacilli," *Dis. of Chest*, 16:661, 1949.
7 Warner, O. W.: "Effect of Varying PAS Dosage in Combined SM-PAS Therapy for Pulmonary Tuberculosis," Eighth Streptomycin Conference, Veterans Administration, Atlanta, Ga., Nov. 10, 1949.
8 Hobby, G. L.: "Effect of PAS Salt of Streptomycin on Experimental Tuberculosis in Mice," Minutes of Seventh Streptomycin Conference, April 23, 1949, Denver, Colorado.
9 Karlson, A. G.: "Effect of PAS Salt of Dihydrostreptomycin on Experimental Tuberculosis in Guinea Pigs," To be published.
10 Adcock, J. C., et al.: "Absorption and Excretion of Streptomycin Para-aminosalicylate," *Proc. of Soc. for Exp. Bio. and Med.*, 72:451, 1949.
11 Harrower, J. R. and Wallace, J. L.: "The Absorption and Excretion of Para-aminosalicylic Acid from SM Para-aminosalicylate," Minutes, Eighth SM Conference, Veterans Administration, Atlanta, Ga., Nov. 10, 1949.

The Chest Survey in a Large General Hospital

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One of the most valuable diagnostic procedures available to the physician is the roentgen examination of the chest. It is probable that more information can be secured from this than from any other single diagnostic procedure. The findings of such an examination are significant in the diagnosis, treatment and prevention of diseases of the cardio-respiratory system; they may determine the operability of distant lesions. Frequently, the existence of entirely unsuspected disease is revealed by this simple process One must, however, bear in mind that it is not an infallible procedure, that the method itself is subject to error, and that the existence of human error on the part of the physician who interprets the radiographs must be admitted. Although I believe that the 14 x 17 inch roentgenographic method of study possesses many points of advantage, the photofluorographic method is almost equally accurate as a screening procedure, and is more readily adapted to the survey of large groups of individuals.

In our hospital three groups of individuals are examined: 1) Inpatients; 2) Out-patients; 3) Employees. We find that pre-employment and annual employee examinations are of great value. In many instances, lesions have been found in pre-employment examinations that were of vital importance to the patient, as well as to the hospital. In particular, we believe that it is important to eliminate tuberculous individuals from that group of potential employees who might have patient contact. The annual chest examination is a procedure that we feel should be adopted by all hospitals, and in a large institution such as ours with over one thousand employees, the photofluorographic survey method of examination is the most practical. The out-patient group includes hospital visitors, who are invited to have this examination without charge, occasional small groups referred by the Marion County Tuberculosis Association, and pre-natal and other pre-admission patients.

It is a well-known fact that cardio-respiratory disease is more common in hospitalized patients than in the general population. The existence of such disease may be the reason for the patient's

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hospitalization, but it is often unsuspected. It is in the group of patients who have unrecognized and sometimes communicable pulmonary disease that examination is of especial importance. The photofluorographic survey procedure is, in most institutions, the most practical method for the study of large groups of individuals, and it is ideal for the examination of hospital admissions.

We do not require that the patient disrobe for the examination, and the procedure requires only a few seconds. The film itself is processed just before noon daily except Saturday, Sunday and holidays, and the interpretation is made by the Radiologist early in the afternoon. The report form for this examination is an integral part of the registration forms; all pertinent data such as name, address, age and sex of the patient are imprinted on this form at the time of admission. The report form we use is almost identical to that which Hodges developed at the University of Michigan; to him I am indebted not only for this but also for much valuable advice at the time of installation of our machine. This formalized report facilitates the radiologists' interpretation of the miniature radiograph, and is readily understood by the attending physician. The same form is used for all examinations, in-patient and out-patient, and the method of examination does not vary. The report lists numerically the most frequent findings: 1) Rib anomaly. 2) Lung anomaly. 3) Acquired bone lesion. 4) Pleural adhesions. 5) Hydrothorax. 6) Tracheo-bronchial lymph node calcification. 7) Parenchymal calcification. 8) Abnormal aorta. 9) Abnormal heart. 10) Mediastinal mass. 11) Pulmonary lesion, definite (this category is reserved for lesions presumed to be tuberculous). 12) Pulmonary lesion, questionable. To balance the two columns of seven items each, as well as offer space for miscellaneous lesions, we have numbers 13 and 14, after which there is a blank space which may be filled in at the time of interpretation.

When he interprets the film, the radiologist places a check mark over the appropriate number to indicate the presence of the particular "finding" which he has observed in the film. The conclusions reached from the examination are listed below the findings, in three categories: A) Negative chest; B) Abnormal chest, no further examination required and C) Abnormal chest, further roentgenographic study definitely indicated. As in the list of "findings," the radiologist interpreting the film checks A, B or C to indicate the "conclusions" he has reached from the examination of this particular film.

The roll of film and the reports are returned to the technician after interpretation. He then distributes the reports as required; personnel reports to the Resident's Office or the Personnel De-

partment, in-patient reports to the appropriate hospital floor, and positive out-patient reports to the Marion County Tuberculosis Association, which contacts both the physician and the patient, if the latter has a lesion suggestive of pulmonary tuberculosis. In addition, the technician "tags" the attending physician's light on the staff attendance board if the Radiologist indicated the necessity for further radiographic study.

If one has facilities for photofluorographic chest survey study available, even for only a brief time, he is certain to become enthusiastic about its merits. I am convinced that this examination is quite as important in the detection of disease as the blood count or urinalysis, and probably more so. This is particularly true, since it may reveal in patients, conditions which are not only important to them, but which may be dangerous to others. The detection of communicable disease is especially valuable in these days when hospital facilities are taxed to the utmost, and to accommodate the patients clamoring for hospital admission it has been necessary to convert single rooms into two-bed rooms or multiple-bed rooms, with consequent over-crowding.

The merit of the miniature film chest survey method and the need for its use having been stablished, the next question relates to its practical application. In the small or moderate size hospital, this should not present insurmountable difficulties. Such institutions are likely to operate under less pressure than the large hospital of over 500 beds. Congestion is not likely to be so troublesome and confusing; distances are not so great as to make one part of the institution relatively inaccessible to others. I have found, however, that in a large, private, general hospital, such as ours, with 700 beds, 23,383 in-patient admissions, and 24,188 out-patient admissions in 1949, the mechanical obstacles are almost insurmountable. As a radiologist, especially interested in pulmonary diseases, I was most anxious to have a survey unit available, and have constantly called to the attention of the staff the tremendous value of the survey method. The medical staff members have been quick to recognize its merit. The hospital administration has cooperated in every possible manner. The State Board of Health has supplied the unit, the technician and the films, without charge; the Marion County Tuberculosis Association has been most cooperative in the following up of out-patient examinations. And still, we manage to survey the chests of a relatively small proportion of hospital admissions. What are the reasons for our failure in this respect? Let us examine the problems inherent in the chest survey study in our large, private general hospital. Many of our patients, 5.8 per cent of the total, are hospitalized for the treatment of traumatic lesions, are seen

briefly in the admitting department, and are sent directly to a room or to the x-ray department. Even with the survey unit in the x-ray department, a majority of such individuals cannot be examined. Many are in shock, and others are extremely uncomfortable and unable to sit or stand up for the chest examination. Another important and large group, 24 per cent of the in-patient registrations in 1949, are the obstetrical patients. Many of these women can be, and are examined, as out-patients in the pre-natal period. If they have not had the benefit of pre-natal examination, it is almost impossible to secure a chest survey study of these patients. Most of them are in labor when they enter the hospital and are transported immediately from the ambulance entrance to the labor rooms. The majority are hospitalized for only five days, and the obstetricians prefer that they not be transported from the obstetrical floor to another department because of the danger of introducing infection to the obstetrical floor. The ambulance drivers who take these patients home, object to even the slight delay involved in the chest filming procedure. A majority of this group of patients is consequently not examined. Another large group of patients whom we fail to examine, are the patients who come in for tonsillectomy; in 1949, they constituted 9 per cent of the total in-patient admissions. These patients are admitted before 7:00 a. m. and are dismissed before the same time the next morning. Tonsillectomy is performed the morning of admission. At first we tried to examine some of these patients in the afternoon, after their surgery. Two or three instances of hemorrhage were encountered, and the otolaryngologists feared that this accident might be attributable to the chest examination, so the policy of post-operative examination was abandoned. A large number of these patients are young children, and it is generally conceded that it may not be essential to examine them. Another group not examined, constitute the medical and surgical emergencies. These patients, whose number cannot be accurately estimated, are so ill on admission that it is too great an effort to have them sit or stand up for the filming procedure. They are usually sent directly to their rooms from the admitting department. A large number of patients are admitted when the technician is not available, coming in after 5:00 in the evening or before 8:00 in the morning, and they are automatically missed unless it is possible to transport them to the filming machine at a later time. I was amazed when Miss Baumann, our Record Librarian, found recently that only 55 per cent of our in-patients are admitted between the hours of 8:00 a. m. and 5:00 p. m. Approximately 13.6 per cent of our admissions in any one year are re-admissions of patients admitted the same year, and if an ad-

mission chest roentgenogram has been secured at some previous admission that year, there is little to be gained by re-examination. If either the patient or the attending physician wishes to have the examination we are always happy to do it.

We have made a conscientious effort to examine as many of the hospital in-patients as possible. When the survey machine was first installed, it was located in the x-ray department which is on the second floor of the hospital, but reasonably close to the registration department, which is on the first floor. This somewhat remote location was at once a disadvantage and an asset. Some patients objected to being detoured through the x-ray department on the way to their rooms; I have since come to believe that their number was small. Hospital visitors and other out-patients were seldom afforded an opportunity to have the chest survey examination, since the equipment was rather far removed from the lobby. The advantage of this initial location was that bed-patients could later be brought to the survey machine for examination, if they were not examined at the time of their admission. The report sheet was in such instances used as a requisition, and examination was requested whenever the patient's condition permitted. Even then, as I reported in a previous communication,[1] we seldom examined the tonsillectomy patients, the traumatic cases, or the obstetrical patients. The problem of the obstetrical patients has been partly solved by the simple expedient of pre-natal examination. Many, but by no means all, of the patients likely to be hospitalized in our institution are referred for chest survey examination as early in the pre-natal period as is possible.

When we decided to move the survey unit, we felt that its location adjacent to the registration office would result in the examination of a larger proportion of in-coming patients. As a consequence, a portion of the lobby waiting room was closed off and has become the chest survey office. Situated just across the hall from the registration department, and immediately behind the information desk, this constitutes an ideal location for the examination of ambulatory patients, hospital visitors, and out-patients in general. We have been surprised and dismayed to find that a relatively small proportion of the in-patients entering a general hospital such as ours can be examined by a unit so situated. Those patients who escape examination on admission cannot later be brought to the machine in the lobby on a stretcher, a procedure which was used to facilitate the examination of many patients when the survey unit was in the x-ray department. The technician problem, while not vitally important, is also to be considered. When the unit was in the x-ray department, we found it relatively

simple to provide a technician to operate the machine, when the regular technician was off duty. With the unit in a more distant location, it has been impossible to provide relief technicians. From the standpoint of number of patients examined, and consequently of community responsibility discharged, the lobby location is ideal. The only objection is that apparently it does not serve to best advantage the original purpose, to secure a survey chest examination of a high proportion of persons being admitted as in-patients.

Until there is a change in the functional design of hospitals, it will be impossible, in the average large, private, general hospital, to secure survey chest film examination of a large percentage of hospital admissions. My experience in the past five years has convinced me that this is true. Regardless of the enthusiasm of the radiologist, the medical staff or the administrative staff, if the physical construction of the hospital makes it difficult to secure such examinations, the proportion of patients who receive this service will be small. My plea, therefore, would be that this matter be given serious consideration in future hospital construction. It is imperative, for this purpose, that the ambulance entrance, admitting department, registration office, photofluorographic unit and x-ray department be in reasonably close proximity to each other.

When the photofluorographic machine was in the x-ray department, many patients who had not been examined at the time of admission, were later brought to the machine on litters or in wheel chairs for the examination. When the condition of the patient permitted, the report form, which is a part of the patient's chart, was initialled by the attending physician or by the resident, and was then sent to us as a requisition for the examination. For some time after we moved the photofluorographic unit to the lobby, we thought it impractical to transport patients to the machine after their admission. We have now concluded that when they are ambulatory, most patients will not object to walking to or being transported in a wheel chair to the hospital lobby. The first item on the physician's order sheet on the chart now is a printed authorization for such examination when the patient is ambulatory. Endorsement of this by the attending physician requires the supervising nurse to send the "Report of admission chest roentgenogram" to the survey technician as a requisition if and when the patient is ambulatory. We hope that this will increase the number of examinations secured, but realize that an immediate admission roentgenogram would be far more valuable than examination at a later period.

Our success with the pre-natal examination has led us to urge

attending physicians other than obstetricians to refer their patients for pre-admission examination. All but the emergency admissions could be examined in this way. In our hospital the patients who are classed as "urgent cases" have to wait 10 days for a room, and "elective cases" may wait several months. The hospital is readily accessible to all sections of the city, and parking facilities are adequate. Our problem is to convince both the patient and the attending physician that the examination is so important as to justify a special trip to the hospital.

I have reviewed in detail the charts of 325 patients in whom re-examination was recently requested and obtained, either on the basis of the "findings" of "11, pulmonary lesion, definite," or "12, pulmonary lesion, questionable." Through the years, we have found that re-examination has been required in 10 to 12 per cent of patients because of findings in these two categories. Fifty-nine of these patients, 2.5 per cent of the total examined, had evidence of pulmonary tuberculosis; these constituted 18 per cent of the patients on whom re-examination was requested. In 32, or 54 per cent of the 59 cases, the existence of pulmonary tuberculosis had not been suspected. While the majority of these were inactive fibroid lesions, recognition of even such tuberculous lesions is important.

There were four false positives, in which the original survey conclusion of a definite or probably tuberculous lesion was not confirmed by a large film re-examination. Two of these patients had primary pulmonary carcinoma of the oat cell variety. In one patient the only finding was apical pleural thickening, and in the other, diagnosis of atypical pneumonia was made.

In the group of questionable and thus probably non-tuberculous pulmonary lesions, 27 large film re-examinations failed to disclose significant abnormality. Re-examination did reveal seven cases of bronchiectasis, three of lung abscess, one complicating a foreign body, eight of pulmonary metastasis and 25 of pulmonary passive congestion, all of which were classified in the survey film interpretation as questionable pulmonary lesions. There were 24 cases of pneumonia, all of the atypical variety, and 10 patients were found to have lesions suggestive of what later proved to be primary carcinoma of the lung. Substernal goitre was found four times. Miscellaneous pathological processes ranging from foreign body atelectasis to pneumonoconiosis, such bone lesions as metastases in the ribs, cardiovascular abnormalities such as cardiac enlargement, myocardial aneurysm, or aortic aneurysm produced such findings in the miniature film as to suggest the need for 14 x 17 inch radiographic examination.

These results certainly attest to the great value of the survey

examination. Many of the lesions whose presence was disclosed by this method would otherwise surely have escaped detection. Many of the cases of pulmonary tuberculosis that we have found were minimal lesions, and probably inactive, but recognition of their existence is important in the medical management of the patients. The survey film method of examination is extremely valuable in the detection of both primary and metastatic cancer of the lung. The evidence of primary pulmonary malignancy may be only suggestive, but this is also true of the large film examination. Certainly all patients in whom the existence of a malignant lesion in any part of the body is suspected should without exception have a survey film examination of the chest on admission to the hospital. The presence of pulmonary metastases can be established as readily by the miniature as by the large film method. Several patients in whom the large film re-examination established the pneumonic character of suspicious pulmonary lesions did not have characteristic clinical evidence of pneumonia at the time of admission, but the disease had been clinically recognized in the majority.

Again, I should like to emphasize the value of the survey method in the recognition of cardiovascular lesions. The ease with which relatively slight cardiac enlargement and evidence of aortic atheromatosis can be demonstrated proves the importance of this method in the early detection of cardiovascular disease. The survey method should be widely used in the program of early detection of heart disease. It is only by early recognition of such abnormalities that we can obtain information about possible etiologic factors such as diet, infection and occupational and environmental influences. If such information were available, its correlation might uncover clues of importance in the development of an adequate cardiovascular disease prevention program.

SUMMARY

1) In the general hospital a photofluorographic chest survey program is ideally adapted to the study of three groups of individuals: (1) In-patients. (2) Out-patients. (3) Hospital personnel.

2) The examination is quickly and easily accomplished.

3) The mechanism of interpretation and reporting are simple.

4) The difficulties inherent in securing examination of a large proportion of hospital admissions are discussed in detail. The importance of hospital design is stressed, and a plea is made that hospitals of the future be so planned that the admission, registration and x-ray departments will be close to each other.

5) Survey examinations reveal positive findings in 10 to 12 per

cent of hospital admissions, and pulmonary tuberculosis in 2 to 3 per cent.

6) The survey method is important in the recognition of other pulmonary pathological processes, and particularly pulmonary malignancy, either primary or secondary.

7) Emphasis is laid upon the importance of the chest survey study in the cardiovascular disease detection and prevention program.

8) No attempt has been made to discuss the economic phase of this method from the standpoint of either original financing or of patient charges.

RESUMEN

1) Un plan de investigación fotofluorográfica es ideal en un hospital general para tres grupos de individuos: (1) En enfermos internados. (2) Enfermos externos. (3) Personal del hospital.

2) El examen es fácil rapidamente efectuado.

3) El mecanismo de interpretación y de informe es sencillo.

4) Las dificultades para procurar un número grande en proporción a las admisiones al hospital se discuten en detalle. La importancia del plan de construcción del hospital se recalca y se sugiere que los hospitales del futuro se planéen de modo que el ingreso, el registro y el departamento de rayos X se encuentren vecinos.

5) La investigación revela hallazgos positivos en 10 a 12 por ciento de los ingresos y la tuberculosis pulmonar en 2 a 3 por ciento.

6) Este método de investigación es importante para el descubrimiento de otros procesos patológicos y particularmente del cáncer primario o secundario.

7) Se hace énfasis sobre la importancia de esta investigación para descubrir las enfermedades cardiovasculares.

8) No se intenta discutir el aspecto económico de esta investigación, ya se trate de la inversión original o del cobro a los enfermos.

RESUME

1) A l'Hôpital, la radioscopie comprend l'étude de trois groupes d'individus: (1) Malades hospitalisés. (2) Malades de consultation. (3) Personnel hospitalier.

2) L'examen est fait rapidement et facilement.

3) L'interprétation est simple.

4) L'auteur discute en détails les difficultés inhérentes à l'examen de contrôle d'une large proportion des malades hospitalisés. Il met l'accent sur l'importance du plan de l'hôpital, et il demande que, dans l'avenir, les hôpitaux soient conçus de façon que l'admis-

sion des malades, leur inscription et le service de radiologie soient proches l'un de l'autre.

5) Les examens systématiques des malades révèlent des lésions chez 10 à 12% des malades admis, et chez 2 à 3%, il s'agit de tuberculose pulmonaire.

6) L'examen systématique est très important pour la mise en évidence d'affections pulmonaires autres que la tuberculose, et particulièrement pour les tumeurs malignes primitives ou secondaires.

7) L'examen systématique du thorax est également très intéressant pour découvrir les affections cardio-vasculaires et en assurer le traitement.

8) Il n'est pas prévu comment ces examens systématiques du thorax pourraient être réglés au point de vue financier.

REFERENCE

1 Ochsner, Harold C.: "The Admission Chest Survey in a General Hospital," *J. Indiana State Med. Assn.*, Sept. 1947, Vol. 40, 869-871.

Cystic Disease of the Lung*

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Probably the earliest reference to pulmonary cysts was made by Thomas Bartholinus in the Leyden edition of Malpighius in 1687.[1] Medical interest however was not aroused and it was not until 1925 when Koontz drew attention to this interesting condition that frequent recognition of the disease began to occur. Koontz was able to collect from the entire world literature only 108 cases to which he added one of his own.[2] Difficulty of diagnosis and diversification of types of pulmonary cysts have materially added to the confusion of both the clinician and the pathologist. Definite clinical or pathological diagnostic criteria cannot be established.

It is the aim of this paper to attempt a simple classification and to describe each variation so that a more frequent recognition of the condition will be possible. In addition seven cases, requiring surgical intervention for relief of symptoms, will be described.

The etiology of pulmonary cysts is in doubt, but it is generally believed that there are two types, congenital and acquired. These are further subdivided into those cysts arising from the bronchial tree and those of alveolar origin. Using conventional terminology a simple classification can be made:

I. Congenital Cystic Disease—congenital cysts or cyst-like cavities of bronchiogenic origin which contain fluid or air.

II. Acquired Pulmonary Cysts—alveolar in origin.
  (a) Blebs
  (b) Pneumatoceles
  (c) Bullae.

III. Cystic Bronchiectasis—congenital (?).

IV. Miscellaneous (not discussed in this paper, includes such entities as true lung abscesses, parasites, trauma, etc.).

I. *Congenital Cystic Disease.*

These cysts vary in size from a millimeter to many centimeters. They may be single or multiple, unilocular or multilocular. Shenck in 1937 collected 381 cases from the literature and found that 38 per cent of the cysts were solitary and 62 per cent multiple. Twenty-three per cent contained fluid and the remainder air.[3] One, two

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

or all lobes may be involved.[4] The lining is usually made up of typical ciliated bronchial epithelium. At times the epithelium is cuboid and even squamous metaplasia may be present. Squamous cell carcinoma has been known to occur under such conditions. Following prolonged infection there is occasionally a complete absence of all epithelium. Fibrous strands lined on all sides by the bronchiogenic epithelium may traverse the cysts, and on occasion are of sufficient thickness to be visible in the roentgenogram.[5] The structure of the wall varies—some are composed of laminated non-descript fibrous tissue while others have smooth muscle, elastic tissue, and even cartilage, but never in the orderly arrangement that occurs in the normal bronchus. This easily differentiates congenital cystic disease from cystic bronchiectasis. In the latter disease the stromal elements of the wall are neat and orderly.[6] Pigmentation can occur in the wall, but apparently this is no basis for the determination of the acquired or congenital nature.[7] Lung tissue in close proximity to the cyst shows varying degrees of compression with infiltration of small round cells and later fibrosis.

Grossly the cyst wall is usually smooth and white or pink, despite the fact that infection may have been present over a long period of time. In every instance there is one or more communications between cysts and adjacent bronchioles. These passage ways are narrow and predisposed to obstruction with ensuing infection. The epithelial lining of the cyst is of the secreting type and material produced can leave only by way of the respiratory tree. The cysts therefore contain fluid or air but if secondary infection has intervened as so often happens the contents may be pus, and if ulceration of mucosa is added blood may be found. Of course any combination is possible.

Symptomatology, assuming the disease is compatible with life at birth, is dependent upon disturbances of intrathoracic pressure by overdistension of the cysts or of suppurative disease following infection of the cysts. Evidence of such complications usually occurs from the first through the third decade. Apparently there is no sex predisposition. Symptoms of overdistension with compression of lung tissue are sometimes confused with spontaneous pneumothorax and in some instances with diaphragmatic hernias. Dyspnea, cough with moderate expectoration, chest pain and cyanosis can occur from resulting changes in pulmonary physiology. Complications such as mediastinal herniation and fatal asphyxia are not uncommon with very large cysts. The distended cyst may have occupied originally only one lobe or a part of a lobe.[8] Suppurative complications are difficult to recognize and are responsible for numerous errors in diagnoses. Chronic empyema is often

an instance of such a cyst.[9] A high index of suspicion is helpful here. Common symptoms are hemoptysis, ranging from severe hemorrhage to slight streaking, cough, moderate expectoration, dyspnea, wheezing, pain in the chest, cardiac palpitation and repeated febrile attacks. In addition obstruction of neighboring bronchioles may predispose to bronchiectasis with added symptoms. The presence of congenital cystic disease of the lung however does not exclude co-existing diseases such as lung abscess, tuberculosis, empyema, carcinoma of the lungs, etc.[10]

A diagnosis of congenital cystic disease of the lung should be based upon a careful chronological history of symptomatology. On this alone many conditions are ruled out. Physical examination with particular attention given to the chest may be of help. In many instances however the findings are equivocal and often disappointing. Radiographic inspection provides the best means of clinical diagnosis. Frequently cysts are visible and easily recognized in the usual x-ray views. In areas which are ill defined and questionable, planigrams can be helpful in determining the presence and location of cysts. When extremely large the x-ray may suggest pneumothorax however hilar shadows are never prominent and often are diminished. When such a cyst contains air alone aspiration of the cyst with re-expansion of the lung followed by an immediate x-ray inspection may reveal the disease. If the cyst contains fluid, aspiration with replacement by air may aid in diagnosis. Either procedure can result in establishing a bronchopleural fistula or pneumothorax, although this rarely happens. Diagnosis often remains in doubt until a biopsy taken at the time of open thoracotomy confirms the previous suspicion. On this basis when draining an empyema, lung abscess, or other suppurative conditions in which any doubt as to etiology is present, biopsy of the cavity wall should be done.

II. *Acquired Pulmonary Cysts.*

(a) Blebs: Pulmonary blebs are collections of air which have localized just beneath the pleura in the interlobular connective tissue. Blebs result from rupture of nearby alveoli which permits air to dissect along the tissue planes of the lungs. The air may remain localized and re-absorb, but in many instances it will rupture through the thin pleura causing spontaneous pneumothorax. On rare occasions it dissects through the hilum of the lung to the mediastinum. The resultant emphysema may be palpated in the subcutaneous tissues of the neck.[11] Little is known concerning the causative agent of pulmonary blebs, especially in the absence of emphysema. Clagget thinks that localized inflammation seals off alveoli in a ball valve fashion, and with excessive

coughing or straining rupture of the alveolar wall occurs. Such conditions as localized bronchiectasis would therefore predispose to their development.[1] The process is acute and little difficulty is encountered in differentiating this from other types of pulmonary cysts. Indeed unless spontaneous pneumothorax results symptoms are minimal. Direct visualization of the ruptured bleb by thoracoscopy is possible when a pneumothorax exists. Most spontaneous pneumothoraces are now considered to be ruptured pulmonary blebs instead of pulmonary tuberculosis as was originally thought. This pneumothorax is usually not of the tension type and leak spontaneously seals over with re-expansion of the lung.

(b) Pneumatoceles: A pneumatocele is a peculiar type of cystic disease. It is essentially a hyperinflated cavity within the pulmonary parenchyma and in contrast to pulmonary blebs is found deep within the tissue. The condition results when an inflammatory involvement of a small branch bronchus serving an area of interstitial pneumonitis establishes a check valve mechanism. The pulmonary segment communicating with the obstructed portion of the bronchial tree is dilated. The increased pressure and primary inflammatory condition synergistically aid in the destruction of intra-alveolar septa. Pneumatoceles usually contain air but may contain moderate amounts of fluid. There is no definite line of distinction between a pulmonary abscess cavity and a pneumatocele.[5]

With the development of a pneumatocele a secondary flare up of the original inflammatory condition is often observed. The clinical picture is not consistent with a large abscess and daily roentgenograms may show fluctuation in size, rapid increase, or perhaps decrease to the point of obliteration. The course of pneumatoceles is usually short lived and for the most part they subside quietly and spontaneously.

(c) Emphysematous Bullae: In generalized pulmonary emphysema, fragmentation of intra-alveolar elastic tissue and rupture of the intra-alveolar septa occurs. This is for the most part a diffusely equal but extensive process. In rare instances this process may occur in a localized part of the lung and the large cavity formed is called a bulla. Again there is probably some obstruction to air passing from the area as in the pneumatoceles, but the obstruction is not constant and increased pressure is only transient as in coughing or straining. Causes of the obstruction may be bronchospasm, infection and allergy.[12]

Bullae may be single or multiple, may or may not communicate with each other. The wall is ill defined and is comprised of destroyed alveolar septa. There is no true epithelial lining and poor communications exist with the bronchi. Therefore infections are

relatively rare. The degeneration and destruction of alveolar walls which caused the bulla predisposes to progression of the disease. Gradual diminution of the ventilatory capacity occurs, hypertension of the pulmonary circuit ensues, and right sided cardiac hypertrophy eventually develops in most cases.

III. *Cystic Bronchiectasis.*

Much doubt exists as to whether this condition is congenital or acquired. Probably it originates as congenital sacculations of the bronchi. This predisposes to localized infection and subsequent dilatation of the saccules. With repeated infection cysts are produced which may range to three or four cms. in diameter. These cysts are found most often in the basilar portion of the lower lobes (dependent areas). A large abnormally dilated bronchus is always found entering the cyst directly, a condition which occurs in no other form of pulmonary cysts.

Microscopically the lining epithelium, typically bronchial, is fairly well retained despite the chronic infection. Ulceration in a few areas is often present. The wall shows thickening, destruction of elastic tissue and infiltration with small round cells. The stromal elements are in an orderly arrangement.

Symptoms are consistent with severe bronchiectasis and little doubt as to diagnosis remains following a bronchogram.

Treatment.

Clinically congenital cystic disease divides itself into an asymptomatic group (possibly discovered by routine x-ray inspection) and a group with symptoms which require the patient to seek medical aid. The presence of a bronchial communication leading to each cyst with alternate periods of drainage and obstruction ultimately results in infection and distension. Active therapy therefore must be instituted in all cases including the asymptomatic. Results are especially good if the complications are minimal or absent. Optimum therapy is to remove the cystic areas if the distribution is not so widespread as to preclude surgery. Depending upon the extent of involvement simple excision of the cyst, lobectomy or pneumonectomy, may be done. Age is no contraindication for small infants withstand pulmonary surgery better than adults, indeed cases are on record of resections in infants only weeks or months of age.[13]

With the first group preoperative preparations are uninvolved and do not differ from other intrathoracic procedures. Roentgenograms should be such that accurate localization of the cystic areas has been accomplished and incision is made accordingly. Once the chest is opened the cysts often spring into immediate view. Despite

this, careful mapping of the entire lung is necessary for the disease is often more extensive than the preoperative x-ray inspections show. This step also will frequently prevent the embarrassment of new cysts appearing in a remaining lobe in a postoperative film. Most surgeons are impressed with the ease of removal before infection has involved any of the cystic areas. Cleavage planes in the hilum are readily established, lymph glands are not enlarged or adherent, and the possibility of pleural contamination by the spillage of purulent secretions is non-existent. Lobectomy is therefore accomplished with little difficulty and with a lower mortality and morbidity than occurs with infected bronchiogenic cysts.

If the disease is bilateral the second side should be operated at a later date. Care is taken to remove as little normal pulmonary tissue as possible, and if simple excision of the individual cysts is feasible this should be done. Postoperative care does not differ from that given lobectomies done for other reasons.

Bronchiogenic cysts which have become secondarily infected provide a greater challenge for the surgeon. Here careful preoperative preparation is imperative for clinical findings correspond in many cases to those of single or multiple lung abscesses. General supportive therapy includes the correction of anemia, hypoproteinemia, and disturbances in fluid and electrolyte balance. Specific measures include the use of antibiotics by either parenteral or oral route as indicated. Occasionally sulfa drugs may be of help. If it has been possible to obtain cultures from the infected area, drug and antibiotic therapy may be directed more accurately. Bronchoscopic examination should include attempts to drain these areas and if endobronchial disease is present it should be actively treated. Aerosol penicillin may be helpful for co-existing bronchiectasis as may postural drainage if bronchial secretions are great. Total removal of these epithelial lined cysts is necessary. Open drainage, trocar drainage or needle decompression are temporary measures and will never result in a permanent cure. Prolonged decompression such as Monaldi drainage is time consuming, expensive and inevitably fruitless. When empyema is established and the spiking temperature shows little response to the measures outlined above, preliminary open thoracotomy and drainage is unavoidable. Definitive surgery is done at a later date. Always at such a procedure biopsy of the empyema wall should be done in order to verify the diagnosis.

With overly distended uninfected bronchiogenic cysts preoperative needle decompression may be helpful and often restores pulmonary physiology temporarily to near normal. If distension is the only complication surgery may be undertaken with little fear. The procedure is the same as with uninfected congenital cysts.

When operating for congenital cystic disease it should be born in mind that other congenital aberrations may be present. The most frequent associated anomaly noted has been a vessel entering the lower lobe through the inferior pulmonary ligament arising directly from the aorta.[14]

Pulmonary blebs as mentioned are fairly acute processes. Following spontaneous pneumothorax which often results from a ruptured bleb the lung will re-expand slowly. The patients should be watched carefully with fluoroscopic or x-ray film inspection from day to day. Occasionally tension pneumothorax develops. This however is a gradual process and either daily aspirations or the insertion of a catheter with continuous gentle suction will suffice to relieve the pressure until the visceral pleura seals over. Major surgery is usually not indicated.

Pneumatoceles are almost medical curiosities, rare indeed, and like pulmonary blebs are self limited. Close observation is necessary once a diagnosis is established. Almost all pneumatoceles close spontaneously. When they fail to disappear but continue to increase in size with associated symptoms, lobectomy is probably the operation of choice.

Bullae, the cysts associated with localized severe emphysema, should first be treated by an attempt to remove the underlying supposedly ball valve inflammatory reaction on the part of the bronchioles or smaller bronchi. Aerosol antibiotics, parenteral drug therapy and a conscientious effort to determine allergy if present are important. If bullae are extensive and totally involve both lungs little can be done. With a single small cyst conservatism is indicated—the patient should be warned of the possible complications and x-rayed at frequent intervals. Dyspnea is the most frequent complaint with a distended cyst and is often completely incapacitating. These are the cases which require vigorous treatment. Needle aspiration is of little help except for emergency relief of profound pulmonary embarrassment. Such a procedure may result in pneumothorax which itself demands treatment. For diagnostic purposes however it may be necessary. If the cyst has ruptured spontaneously resulting in pneumothorax, therapy is the same as with pulmonary blebs. After re-expansion the patient is carefully evaluated and the necessity for surgery decided upon. If the lung fails to remain expanded, open thoracotomy with excision of the area or repair of the defect gives good results.

In the majority of cases symptoms result from a large solitary cyst which occupies a part or all of the pleural cavity. Here operative removal is most gratifying. Often by simple excision or lobectomy a respiratory cripple may be changed into a moderately active person. If patients with large bullae are in such critical

condition that major surgery is impossible intracavitary drainage of the Monaldi type may be used.[15] The technique is relatively simple. Under local anesthesia an extrapleural dissection is made to determine presence or absence of pleural symphysis. If symphysis has not occurred as is usually the case fusion is initiated by placing an oxycel gauze pack in approximation with the parietal pleura.[16] The pleurae are firmly adherent in 10 to 14 days when the second stage is performed. At this time the catheter is placed deep in the cyst and skin edges around the catheter made air tight. It is then connected to a water sealed bottle. If x-ray films show little obliteration of the cyst after a few days, gentle suction is applied until the cyst has disappeared and adjacent atelectatic lung is fully expanded. With such a procedure the use of antibiotics throughout the entire course is necessary. Results with this form of treatment are often surprisingly good.

Cystic bronchiectasis demands the same treatment severe bronchiectasis of other types is accorded. Proper preoperative preparation followed by complete surgical excision of the involved areas, bilateral if necessary, will result in dramatic relief of symptoms.

Case Reports

Case 1: E.A.S. A 56-year-old white male was admitted to Veterans Administration Hospital, Oteen, N. C. on October 25, 1948, with a chief complaint of cough and dyspnea. Chronic cough had been present since 1918. The cough was productive during periods of respiratory infection. Several years prior to admission he noticed shortness of breath on exertion which gradually became worse. In February 1948 there occurred a sudden sharp pain in his right chest accompanied by severe dyspnea. He was admitted to another hospital with a diagnosis of spontaneous pneumothorax. Repeated studies of the sputum and frequent x-ray inspections were made, but he was not apprised of the results. He was discharged in May 1948 but continued to feel weak and the cough increased in severity. By October 1948 dyspnea was extreme and his cough was productive.

Physical examination on admission showed a well nourished white male with moderate dyspnea. Examination of the chest revealed diminished expansion on the right. Increased tactile fremitus, impaired resonance and fine medium inspiratory rales were noted posteriorly. The left lung was normal. The remaining physical examination revealed nothing of note.

Initial chest x-ray inspection showed hyperventilation of the right lung and a definite cystic area about 5 cm. in diameter in the apex (Fig. 1a and 1b). Laboratory data: Complement fixation for syphilis was negative, urine negative, RBC 5,000,000; HBG 105 per cent; WBC 13,000, with 73 neutrophils, 22 lymphocytes, two monocytes, three eosinophils. Vital capacity was 2600 with a normal of 4350.

He was placed on supportive therapy, prepared for operation, and on December 7, 1948 a right thoracotomy was done. When the chest was opened multiple cysts in all lobes were palpated. Two exceptionally large bullae were present in the apex and were opened when attempting to dissect the visceral from the parietal pleura. These cysts were excised

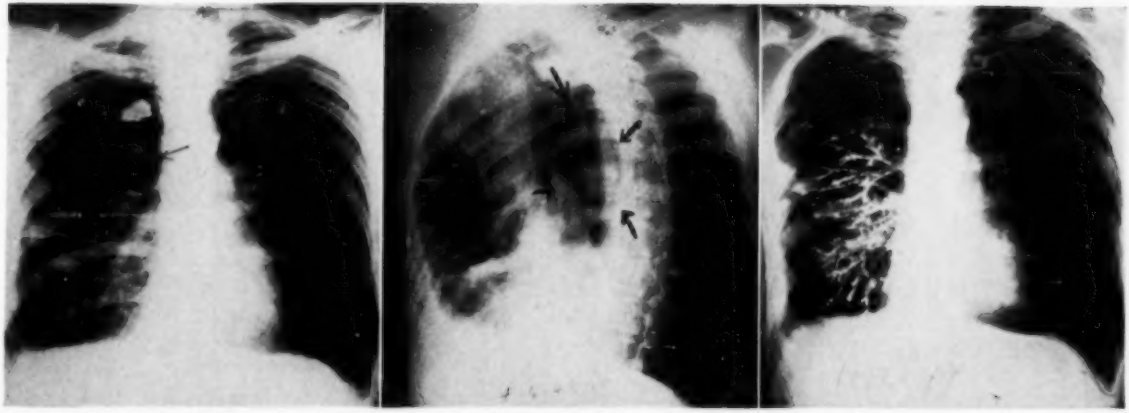


FIGURE 1a FIGURE 1b FIGURE 1c

Fig. 1a: Large emphysematous bulla in right apex. Middle and lower lobes are compressed and the diaphragm is lowered. — *Fig. 1b:* Left anterior oblique view of same cyst showing the typical spherical appearance. — *Fig. 1c:* Bronchogram following removal of the cystic areas in apex. Compression of lower and middle lobes is no longer present. Patient experienced marked relief of dyspnea.

and two additional smaller cysts were also removed. The lung bed from which the cysts were removed was closed from the bottom up with fine catgut suture. The patient had an uneventful postoperative course and marked relief of symptoms was noted (Fig. 1c).

The pathological report was as follows: The specimen consisted of two pieces of irregularly thickened pleura, the largest measured up to 7 cms. in length. Microscopically broad fibrous layers of subpleural tissue with hyperemia and lymphocytic infiltration was present. Attached to one piece was a narrow layer of hemorrhagic lung tissue. Diagnosis: Wall of emphysematous bullae with low-grade chronic nonspecific pleuritis.

Case 2: J.C.C. A 24-year-old white male who was apparently in good health until February 1948 when he developed a severe cold and cough which did not improve under symptomatic therapy. For two or three days prior to admission on April 16, 1948 the sputum had been blood streaked. No weight loss had been experienced but occasional right sided pain was present.

Physical examination on admission showed a well developed, well nourished white male, not appearing acutely or chronically ill. Chest: No limitation of expansion, normal tactile fremitus, normal breath sounds with no change in whispered or spoken voice. No rales were present. Remainder of physical examination showed no abnormality.

Initial x-ray films revealed right lower pneumonitis and a cystic area near the cardiac border. This contained fluid and air. Exhaustive sputum studies for acid-fast and fungus organisms were negative. Laboratory studies showed urine negative, complement fixation test for syphilis negative, a blood count of RBC 5,500,000 with 91 per cent HBG; WBC 6,100 with a normal differential. Vital capacity was 3050 with a normal of 4500.

He was placed on general supportive therapy. On April 29, 1948 bronchoscopy was negative except for rather tenacious white mucous seen exuding from the right lower lobe orifice. Bronchograms done a few days later showed no bronchiectasis and no communication of the bronchi with the cavities was observed. A tentative diagnosis of congenital cystic disease was made and on September 23, 1949 at exploratory thoracotomy three large cysts were felt in the lower lobe. The lobe was removed uneventfully. The patient withstood the procedure well and recuperated rapidly. There was complete relief of symptoms.

Pathological examination revealed the lower lobe of the right lung measuring 14 x 12 x 3 cms. with a soft and meaty consistency. The pleura was opaque. The lobar bronchus was severed after its division. Hilar lymph nodes were soft, black, and did not exceed 1 cm. in length. In following the medial basal bronchus for 3 cms. a honeycombed cavity, apparently lined with bronchial mucosa and traversed by vascular bridges, was entered. The cavity reached down to the base and had a maximum transverse diameter of 4 cms. Other bronchi were not remarkable. The lung tissue was non-aerated. A branch of the original bronchus leading posteriorly communicated with the cavity. Microscopically sections from the cavity wall showed a lining of typical respiratory epithelium supported by dense fibrous tissue containing small groups of lymphocytes and plasma cells. Despite the chronic infection and fibrosis orderly histological arrangement was noted. A diagnosis of congenital saccular bronchiectasis was made.

Case 3: J.D. A 52-year-old white male was apparently in good health until December 1945 at which time he developed bilateral pneumonia for which he was treated in Jacksonville, Florida. During the treatment he developed spontaneous collapse of the left lung which re-expanded without aspiration. Since then exertional dyspnea has been present and a slightly productive cough, most evident in the morning, also noted. Symptoms progressed until August 1947 when he was told by his private physician that he had a large cyst in the right upper lobe. On the advice of this physician he was admitted to Veterans Administration Hospital, Oteen, N. C. on March 31, 1948 with a chief complaint of dyspnea on slightest exertion. Recent weight loss, weakness and occasional pain in right lower chest were also present.

Physical examination showed a farily well developed, well nourished white male in no acute distress. Examination of the chest was negative except for a few wheezes in the right apex. No rales were heard. Percussion was normal and no changes in fremitus were present. X-ray film showed the entire upper lobe to be occupied by a large cyst with a thin wall and no surrounding reaction. The remainder of the lung appeared clear (Fig. 2a). Studies for tuberculosis were negative. Laboratory data: Urine negative, complement fixation test for syphilis negative, blood count within normal limits. At exploratory thoracotomy April 27, 1948 two large cysts (Figs. 3a and 3b) on the anterior and the posterior medial portion of the upper right lobe were present. The posterior cyst was 18 cms. in diameter and both contained air. They were opened, the wall excised and the parenchyma approximated and sutured. After the lung was re-expanded the chest was closed. Uneventful convalescence followed and marked relief of symptoms was experienced (Fig. 2b).

Pathological examination: The specimen consisted of five portions of cyst walls, the largest measured 12 x 19 cms. The membranes were paper thin and smooth with pin-point hemorrhages on one side and vascular ridges on the other side. Microscopically the cyst wall was formed by hyperemic connective tissue that in places showed hyalinization of fibers and in others a loose infiltration with plasma cells and lymphocytes. It

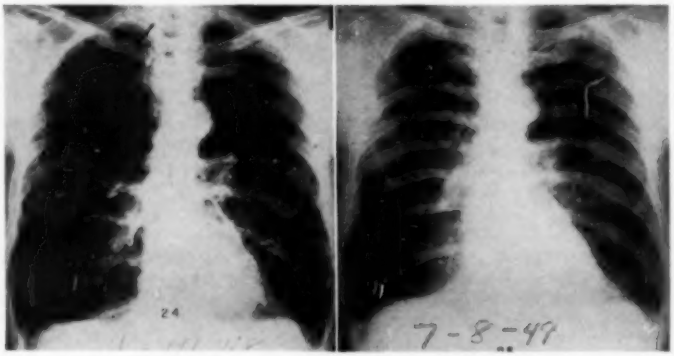


FIGURE 2a FIGURE 2b

Fig. 2a: A congenital cyst occupying the upper one-third of the right pleural cavity.—*Fig. 2b:* Complete re-expansion of remaining lung tissue after removal of the cyst.

was lined by a single row of cuboidal epithelial cells. No elastic fibers or cartilage were seen in the cyst walls. A diagnosis of congenital cysts of the lung was made.

Case 4: J.H.A. A 27-year-old white male who entered the hospital on July 24, 1947 with a chief complaint of dyspnea and onset of sudden severe pain in left chest. He was apparently well until early in 1946 when he had slight weight loss and noticed easy fatigability. This continued until April 1947 when he had several episodes of hemoptysis consisting of streaking of mucoid sputum. In June he developed sudden pain in the left chest following an attack of severe dyspnea. Pain became worse and he was hospitalized for several days with a diagnosis of spontaneous pneumothorax. He apparently improved and was discharged. On admission here chest pain was present and exertional dyspnea marked.

Physical examination on entrance showed a well developed, well nourished white male not appearing acutely or chronically ill. In the left thorax tactile fremitus was diminished and breath sounds were distant, especially at the base. No posttussive rales were heard. The remaining physical examination was essentially negative. X-ray inspection revealed about 25 per cent collapse of the entire left lung and an area of radiotranslucency in the left base with a fluid level. Laboratory examination: Urine negative, Kahn test negative, blood count within normal limits. Vital capacity was 2450 with a normal of 4300.

On August 12, 1949 thoracotomy was accomplished entering through the bed of the eighth rib. Immediately a large cyst approximately 8 cms. in diameter was seen in the lateral inferior portion of the lower lobe. It was adherent to the diaphragm and in several areas there was nodular thickening on its outer wall. In addition there were several smaller cysts in the thin inferior portion of the lower lobe. The large cyst was opened and saline instilled. No bubbling occurred with an increase in intratracheal pressure. The wall of the cyst was excised and the bed closed with a fine continuous suture of chromic catgut. Two other cysts in the same lobe were excised in a similar manner and the chest was closed. An uneventful postoperative course ensued. He no longer had exertional dyspnea.

Pathological examination: The specimen consisted of a cystic oval mass 5 x 2½ cms. and half filled with fluid. Along one lung edge ran an irregular blood colored piece of tissue with clamp marks while on the opposite side the smooth outer wall (pleura) was interrupted and showed lung tissue 7 mm. wide. On opening the cyst it was found that the lumen was traversed by delicate tissue masses from which foamy, pale, blood colored fluid exuded. Also present was a membranous piece of tissue 4 x 5 cms. and 1-3 mm. thick. The thicker portions were of cartilaginous consistency. Microscopically the subpleural layer of fibrous tissue was markedly thickened and in places it consisted of coarse hyaline fibers. The lung tissue showed varying degrees of alveolar enlargement. Diagnosis: Emphysema and fibrosis of lung with cyst formation.

Case 5: E.W. A 51-year-old white male, who had suffered from asthma all of his life, entered the hospital on May 13, 1947 with a chief complaint of dyspnea. He had controlled his asthma fairly well until March 1947 when he developed a chilly sensation following a heavy cold. He suddenly became rather dyspneic. With the onset of this dyspnea his previous unproductive cough began producing yellow mucoid material. He

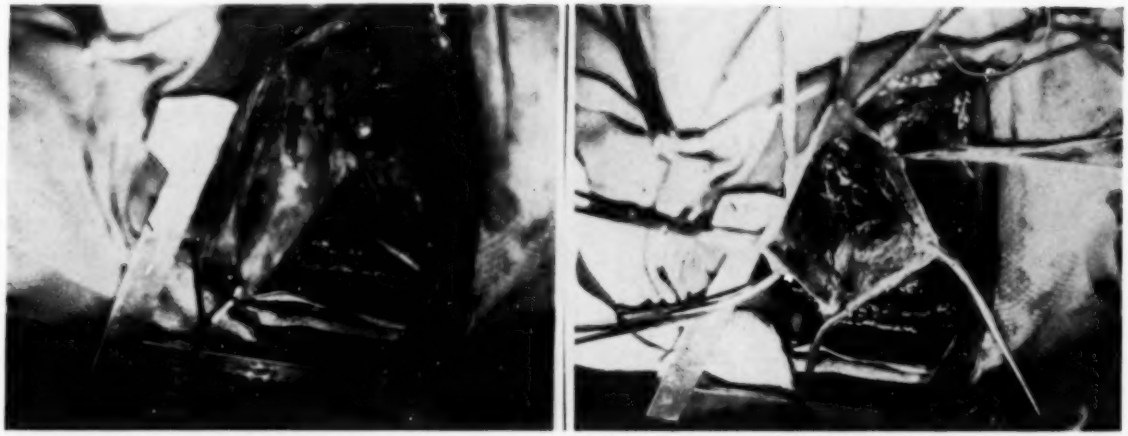


FIGURE 3a

FIGURE 3b

Fig. 3a: Appearance of the cyst when the chest was opened.—*Fig. 3b:* With cyst opened the loculated inner surface and traversing fibrous strands are clearly seen.

consulted his family physician and a few days later was sent to the Veterans Administration Hospital in Johnson City, Tennessee where pneumothorax on the right was discovered. He was treated with antibiotics and aspirations but the lung failed to re-expand. He was then referred to Veterans Administration Hospital, Oteen, N. C. for further treatment.

Physical examination: He was fairly well developed, somewhat undernourished, appearing in rather acute respiratory distress but well oriented and cooperative. Chest examination showed limitation of expansion on the right, absent tactile fremitus, and hyperresonance to percussion. Breath sounds were absent. The left lung was normal except for exaggerated breath sounds and a few posttussive rales heard at the left base. A catheter was inserted May 14, 1947 into the right pleural space and continuous gentle suction applied. By May 20, 1947 the lung was fully expanded and x-ray films now showed a large oval shaped area of radiolucency just above the right diaphragm (Figs. 4a and 4b). It has a well demarcated upper and lateral wall but its lower wall merged with the shadow of the diaphragm. Bronchoscopic examination on June 2, 1947 was negative. On June 10, 1947 after preoperative preparations the patient underwent an exploratory thoracotomy. The eighth rib was resected and the chest opened. Numerous adhesions of the parietal and visceral pleura were present. By blunt dissection the lung was separated from the chest wall. Its base was adherent to the diaphragm and adhesions were separated by a combination of sharp and blunt dissection. There was a loculated, air-containing cyst on the base of the right lower lobe which could be distended at will by the anesthetist. The cyst was opened and found to be connected with the alveoli in several places. The wall of the cyst was excised and the lung was sutured with a locked stitch of fine chromic catgut. The closure was air tight as tested by positive pressure. He had an uneventful postoperative course and marked relief of symptoms (Fig. 4c).

Pathological report: Specimen consisted of four pieces of membranous tissue. The largest was 8 cms. in length and 2 cms. wide. One surface was smooth, dark and rough, and the other was ragged. Microscopically: Pleura with a broad subserous fibrous layer, partly vascular partly dense, was noted. One portion was infiltrated with round cells and plasma cells and contained anthrocotic and phagocytized blood pigment. Diagnosis: Emphysematous Bulla.

Case 6: J.P.B. A 52-year-old white male was admitted on March 19, 1947 with a chief complaint of cough and weight loss. He was apparently well until 10 years prior to admission when he developed a slightly productive cough which persisted. In February 1947 he experienced sudden pain in the left chest followed by fever and malaise. He entered another hospital at that time and was told that he had a collapsed left lung. No evidence of tuberculosis or malignancy could be found. Following discharge his cough, expectoration, dyspnea, and gradual weight loss continued. At time of admission here he had developed severe dyspnea with the slightest exertion and his cough was productive of one-half cup of mucoid greenish material per day. Only on one occasion did he cough blood.

Physical examination: Well nourished, well developed white male appearing chronically ill. Chest examination showed hyperresonance over the left lung and dullness in the lower half. Occasional moist rales were also heard in the left apex. The right lung was clear. No other abnormal

FIGURE 4a FIGURE 4b FIGURE 4c

Fig. 4a: Preoperative appearance of emphysematous bulla in right lower lobe.—*Fig. 4b:* Lateral view showing antero-posterior diameter of the cyst.—*Fig. 4c:* Postoperative appearance following simple excision of the emphysematous bulla.

physical findings were present except for bilateral herniorrhaphy scars. Initial chest film showed generalized emphysema with an area of translucency in the left apex (Fig. 5a). Studies were negative for fungi and tubercle bacilli. He was prepared for thoracotomy and on May 1, 1947 the left chest was opened. A large cyst approximately 12 cms. in diameter was immediately seen in the upper lobe. A manometric pressure reading was taken and found to be plus one. Any increase in intratracheal pressure did not increase the pressure in the cyst. The cyst was then opened and its walls were found to be of compressed lung tissue. Saline was introduced into the cyst and intratracheal air pressure increased. Small but numerous bubbles were seen indicating many connections with the outer alveoli of the lung but no direct connection to the bronchi. The thin cyst wall was excised down to normal lung tissue and this was then closed with a running locked suture of fine chromic catgut. No other cysts were noted. He had an uneventful postoperative course and when he left the hospital had no dyspnea on exertion.

The pathological report showed two membranes measuring 5 x 17 cms. and 8 x 8 cms. One side of the membrane was smooth, the other was dull and showed relief of injected blood vessels. Microscopically the membrane consisted of pleura with preserved mesothelial covering. Attached was a flat piece of lung tissue in which fibrosis and round cell infiltration were seen. Alveolar spaces were partly compressed and partly dilated. Diagnosis: Emphysematous Bulla.

Case 7: C.A.C. A 31-year-old white male was admitted to Veterans Administration Hospital, Oteen, N. C. on May 12, 1948 with chief complaints of hemoptysis, dyspnea and weight loss. He was apparently well until 1944 when in New Guinea he developed chest pain, cough and fever. He was hospitalized for 10 days and a diagnosis of chronic bronchitis was made. Several months later a similar episode occurred and he was told he had bronchiectasis. In 1944 while in Florida he had a third attack. Bronchoscopy was done and bronchograms made. Chronic bronchitis was again diagnosed. Shortly thereafter he received a medical discharge

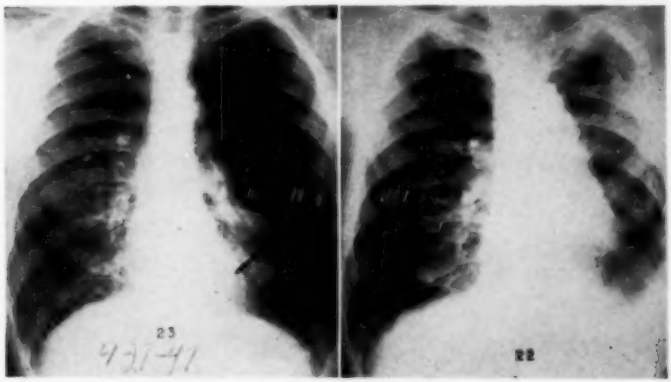


FIGURE 5a FIGURE 5b

Fig. 5a: Emphysematous bulla occupying a large portion of the left chest.—*Fig. 5b:* Postoperative expansion of remaining lung tissue.

from the army. He continued to have a productive cough and in 1947 after a visit to a medical center he was again hold he had bronchiectasis. In January of 1948 he began to lose weight, his cough became more productive (one-half cup mucoid sputum daily), and temperature elevations to 102 degrees began to occur. On admission to the Veterans Administration Hospital in Fayetteville, N. C., pneumonia was present and he was treated with penicillin. Response was rapid and following recovery a bronchogram revealed bronchiectasis of all lobes of both lungs. After discharge dyspnea was noticeable and increased. Shortly before admission to Oteen Hospital his dyspnea became severe and some hemoptysis was present. Weight loss had amounted to about 15 pounds.

Physical examination on admission revealed a young white male, not appearing acutely ill. Moderate dyspnea was present. The chest displayed the typical barrel shape of chronic emphysema. Expansion was equal bilaterally and diminished. The percussion note was generally hyperresonant. Vocal fremitus was normal and posttussive rales were heard throughout both lungs. Clubbing of the fingers was also noted. Admission x-ray film showed generalized far advanced emphysema with a large cyst of the right lower lung (Fig. 6a). He was placed on aerosol and parenteral penicillin with slight improvement. On May 21, 1948 hemoptysis occurred for a short period and by June 2, 1948 bronchopneumonia had developed in the right lower lobe. This began to clear shortly but dyspnea became severe and little response was shown to high concentrations of nasal oxygen. Additional measures were necessary. On June 8, 1948 under local anesthesia a trocar was introduced on the right through the 10th interspace and anterior axillary line. A catheter was passed into the cyst (Fig. 6b). About 200 cc. of chocolate fluid immediately poured out. Continuous gentle suction was applied. Soon after its introduction the cyst became smaller in size and by June 16, 1948 was not visible on x-ray film. Catheter was removed on June 30, 1948.

Following resolution of pneumonia and obliteration of cyst this patient improved slightly. Mild dyspnea however was constantly present

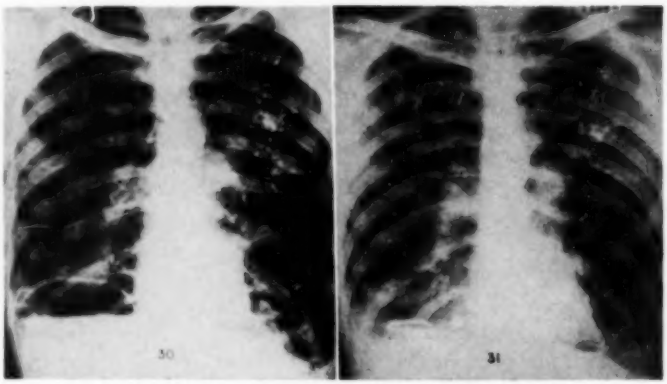


FIGURE 6a FIGURE 6b

Fig. 6a: Large fluid filled emphysematous bulla in right lower lobe.—*Fig. 6b:* Disappearance of cyst following Monaldi drainage. Catheter is still in place.

and even mild exertion was impossible. He is still a respiratory invalid with severe general bronchiectasis and far advanced emphysema.

SUMMARY

1) A simple classification of cystic disease of the lung is presented. Three major groups are defined: (a) Cysts of bronchial origin; (b) Cysts of alveolar origin; (c) Cystic bronchiectasis of a congenital nature.

2) A detailed description of the symptomatology, clinical and x-ray findings, gross and microscopic descriptions of each variation of cystic disease has been outlined.

3) Treatment including both supportive and definitive types is suggested. Therapy yielding best results in our hands has been operative removal of the cystic areas when feasible. With poor risk patients, Monaldi drainage may be of benefit.

4) Seven consecutive patients with cystic disease of the lung have been presented. All had surgical therapy of some type. In six the results were good. One patient failed to respond because of other co-existing pulmonary disease.

RESUMEN

1) Les auteurs proposent une classification simple de la maladie kystique du poumon. Trois groupes essentiels sont individualisés: (a) les kystes d'origine bronchique; (b) les kystes d'origine alvéolaire; (c) les bronchectasies kystiques de nature congénitale.

2) Se describe la sintomatología, los hallazgos clínicos y radiológicos, aspectos macro y microscópicos de cada variedad.

3) Tanto el tratamiento auxiliar como el definitivo se sugieren. El tratamiento más efectivo en nuestras manos ha sido la extirpación quirúrgica cuando es practicable. Con los malos riesgos el drenaje de Monaldi puede ser útil.

4) Se presentan siete casos consecutivos de enfermos con enfermedad cística del pulmón. Todos han sufrido alguna terapéutica quirúrgica. En seis los resultados fueron buenos. En uno el tratamiento fracasó por la coexistencia de otra enfermedad pulmonar.

RESUME

1) Les auteurs une classification simple de la maladie kystique du poumon. Trois groupes essentiels sont individualisés: (a) les kystes d'origine bronchique; (b) les kystes d'origine alvéolaire; (c) les bronchectasies kystiques de nature congénitale.

2) La symptomatologie en est étudiée en détails avec, pour chaque catégorie de kystes les manifestations cliniques et radiologiques, et les descriptions macroscopiques et microscopiques.

3) Le traitement est envisagée en fonction des types cliniques. Les auteurs estiments que les meilleurs résultats ont été obtenus quand l'exerèse du territoire kystique a pu être réalisé. Dans certains cas les malades ont pu bénéficier d'un drainage à la Monaldi qui n'entraine pour eux aucun risque.

4) Sept observations de malades atteints de maladie kystique du poumon sont rapportés. Tous ont été l'objet d'une intervention chirurgicale. Dans six cas les résultats furent bons. L'échec du 7ème cas est imputable à une autre affection pulmonaire coexistante.

REFERENCES

1 Clagett, O. T.: "Surgical Treatment of Emphysematous Blebs and Bullae," *Dis. of Chest*, 15:669, 1949.
2 Koontz, A. R.: "Congenital Cystic Disease of the Lungs," *Bull. Johns Hopkins Hosp.*, 37:340, 1925.
3 Shenck, S. G.: "Diagnosis of Congenital Cystic Disease of the Lung," *Arch. Int. Med.*, 60:1, 1937.
4 Ravitch, M. M. and Hardy, J. D.: "Congenital Cystic Disease of the Lung in Infants and in Children," *Arch. Surg.*, 59:1, 1949.
5 Adams, W. E.: "Differential Diagnosis and Treatment of Congenital Cystic Malformations of the Chest," *Dis. of Chest*, 15:60, 1949.
6 Dickson, M. D., Clagett, O. T. and McDonald, J. R.: "Cystic Disease of the Lungs and Its Relationship to Bronchiectatic Cavities," *Jour. Thoracic Surg.*, 15:196, 1946.
7 Moersch, H. J. and Clagett, O. T.: "Pulmonary Cysts," *Jour. Thoracic Surg.*, 61:179, 1947.
8 McGarth, E. J. and Magnussen, M. H.: "Cystic Diseases of Lung," *Arch. Surg.*, 57:427, 1948.
9 Maier, H. C. and Haight, C.: "Large Infected Solitary Pulmonary Cysts Simulating Empyema," *Jour. Thoracic Surg.*, 9:471, 1940.
10 Menefee, E. E. Jr.: "Cystic Lung Disease," *North Carolina Med. Jour.*, 10:184, 1949.
11 Freedman, E.: "Emphysematous Blebs and Bullae," *Am. Jour. Roentg.*, 35:324, 1936.
12 Barnett, W. E.: "Cystic Emphysema of the Lungs," *Arch. Surg.*, 58: 328, 1949.
13 Gross, R. E.: "Congenital Cystic Lung: Successful Pneumonectomy in a Three-Week Old Baby," *Ann. Surg.*, 123:229, 1946.
14 Meade, Richard H. Jr.: "Cysts of the Mediastinum and Lungs," *Kansas City Med. Jour.*, 22:17, 1946.
15 Head, J. R. and Avery, E. E.: "Intracavitary Suction (Monaldi) in the Treatment of Emphysematous Bullae and Blebs," *Jour. Thoracic Surg.*, 18:761, 1949.
16 Murphy, J. D. and McDaniel, J. R.: "The Use of Oxidized Cellulose in Pleural Symphysis," *Jour. Thoracic Surg.*, 17:416, 1948.

Pulmonary Manifestations of Systemic Diseases*

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A number of apparently non-infectious systemic diseases frequently, but by no means invariably, give rise to pulmonary lesions. Among these are: rheumatic fever, rheumatoid arthritis, periarteritis nodosa, lupus erythematosus, scleroderma, and erythema nodosum. Other diseases with pulmonary manifestations, such as Loeffler's syndrome and sarcoidosis, are too broad in scope for this discussion.

Scleroderma: The pulmonary fibrosis occurring in scleroderma is one of the most widely recognized pulmonary manifestations of the diseases listed above. Pathologically, there is progressive interalveolar sclerosis, collagen fibers replacing the elastic tissue normally present. The alveolar walls may disintegrate, especially at the periphery, giving rise to a cystic appearing condition.[9]

Dyspnea on even slight exertion is the most frequent symptom.[13,24,25] There may be a cough, at times productive of whitish mucoid sputum. Physical findings are usually limited to decreased resonance and inconstant fine moist rales, particularly in the bases. The typical roentgenogram exhibits a diffuse granulation or mottling, particularly at the base, extending well out to the periphery, but sparing the apices.[24,25] There may be peripheral cystic changes.[5]

Illustrative Cases: 1) K.W. 14926C, white female, age 30. There were no pulmonary symptoms. On physical examination there were a few coarse moist rales at both bases posteriorly (Fig. 1).

2) J.C.H., white female. Dyspnea marked, attributed to heart failure. Physical findings in lungs not recorded. Diagnosis: generalized scleroderma (Fig. 2).

Lupus Erythematosus: Pulmonary findings are less frequent in lupus erythematosus. Clinically, there is a patchy to confluent pneumonia, frequently complicated by secondary invaders. This pneumonia, like all the other manifestations, has the characteristic pathohistological features,[19] which need not be reviewed here. In at least one reported instance,[1] the chest x-ray was considered suspicious of tuberculosis, and I have seen another,

*From the Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas. Read at the annual meeting, Texas Chapter, American College of Chest Physicians, Fort Worth, May 1, 1950.

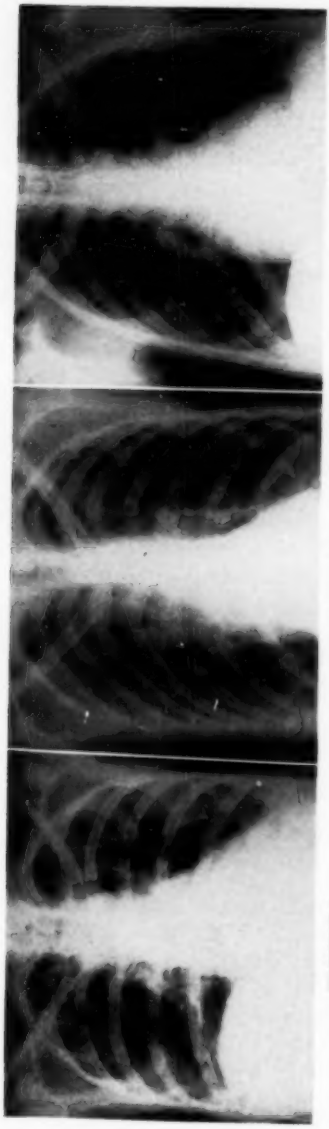


FIGURE 3

FIGURE 2

FIGURE 1

diagnosed as lupus erythematosus by biopsy, accepted on a tuberculosis service on the basis of clinical and x-ray findings, although the bacteriological examinations of the sputum were consistently negative for tubercle bacilli.

X-ray changes are frequently present, but are not sufficiently characteristic for diagnostic purposes.[20]

Illustrative Case: M.E.W. 5440D, colored female, age 24. There was a cough for several weeks prior to admission, productive of small amounts of thick white sputum. On the day of admission there was a small hemoptysis. On physical examination there were crepitant rales in both bases. The patient died on the 13th hospital day. Post-mortem diagnoses were: lupus erythematosus; bronchopneumonia, bilateral; pleural effusion, bilateral, 400 cc. Chest x-ray on the day of death was reported negative (Fig. 3).

Periarteritis Nodosa: In a comprehensive review of a large number of cases of periarteritis nodosa, pulmonary lesions were said to be uncommon.[3] However Sweeney and Baggenstoss[22] report parenchymal lesions, with characteristic changes in the vessels of the lungs and bronchi, in eight of 28 cases (28 per cent) and cite other series with incidences of 25 and 29 per cent.

Microscopically, in addition to the vascular changes, there may be perivascular pneumonia, with similar lesions apparently dissociated from the vessels. Granulomatous lesions, also seemingly independent of the vascular changes, were noted.[22]

Many patients have no pulmonary symptoms, although bronchial asthma, increasing in severity, has initiated the syndrome in some cases; in others weight loss, fever, cough, and expectoration of blood has led to an erroneous diagnosis of tuberculosis.

The physical and x-ray findings are in general said to be variable and not diagnostic.[3,6,21,22] One writer mentions transitory pulmonary infiltrations, in the absence of heart failure, strikingly similar to the findings in Loeffler's syndrome.[15]

(For the sake of brevity, discussion of such complications as pulmonary infarction and pleuritis has been omitted).

Illustrative Case: W.B. 4682F, colored male, had no pulmonary symptoms on admission; lung fields were normal on physical examination. Later there were fine moist rales at both bases posteriorly. The patient died two months after admission with an acute myocardial infarction. Post-mortem findings included an "organized pneumonia," not further described in the protocol. The admission x-ray film is shown (Fig. 4).

Rheumatic Fever: The occurrence of true rheumatic pneumonia is controversial.[8,10,17] In many instances there is found post-mortem a pulmonic consolidation containing many large cells resembling those of rheumatic granulomata.[4] Rich[18] attributes the changes to focal damage to the pulmonary capillaries, basic-

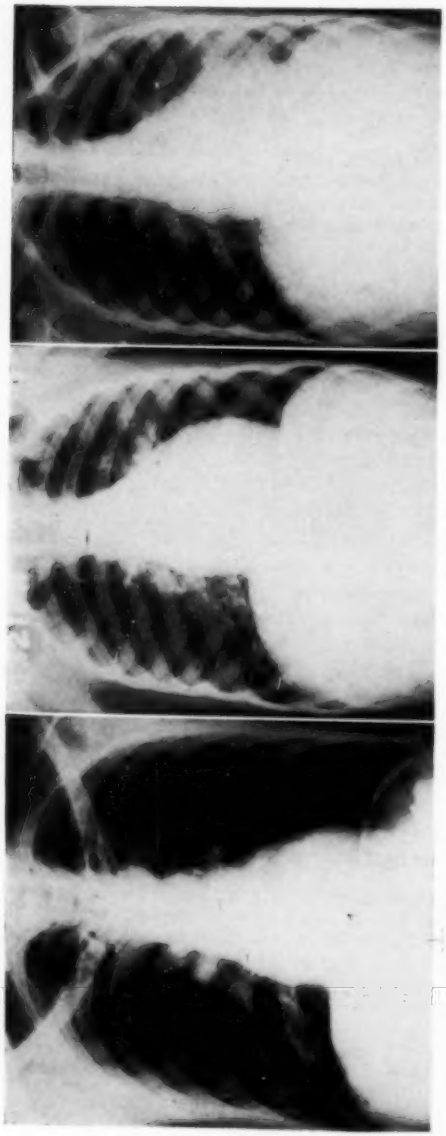


FIGURE 6

FIGURE 5

FIGURE 4

ally identical with sulfonamide sensitivity pneumonitis. Regardless of whether the lesion is specific or not, there is a characteristic pulmonary picture, consisting of alveolitis, marked congestion, edema, engorgement, and the formation of hyaline membranes.

Clinically, the signs of pulmonary involvement are hard to interpret, due to frequently accompanying pleural effusions, pericardial exudates, or a dilated heart. A fleeting pneumonitis, evidenced by either signs of frank consolidation, or by scattered rales and diminished breath sounds, should give rise to the suspicion of this complication, provided there is no evidence of myocardial insufficiency.

The x-ray findings are variable, being interpreted as intense congestion, edema, pneumonitis, infiltration, infarct, or pneumonia.

Illustrative Case: S.P. 10321F, white female, age 10, was admitted October 10, 1949, with active rheumatic fever. There had been a previous episode three years earlier. There were no pulmonary symptoms; no abnormal lung findings by physical examination were recorded during her stay. There was no evidence of myocardial failure. Chest x-ray films on October 26, 1949 (Fig. 5), and October 29, 1949 (Fig. 6), showed a shifting involvement on the left. Another film a few weeks later showed complete clearing. On the basis of the changing x-ray findings, a diagnosis of rheumatic pneumonitis was made.

Rheumatoid Arthritis: Recently, pulmonary lesions in cases of rheumatoid arthritis have been reported[7,12] with the suggestion that we refer to "rheumatoid disease."

One case, without pulmonary symptoms, had diminished breath sounds and crepitant rales in both bases. The radiological report was "fine reticulation throughout both lungs and a chronic bron-

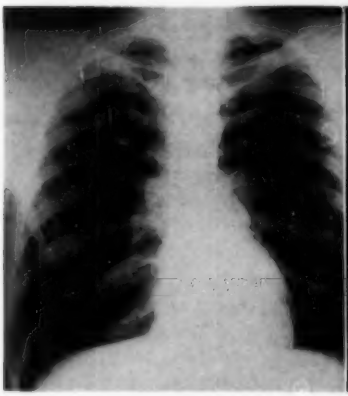


FIGURE 7



FIGURE 8

chopneumonic lesion." Post-mortem examination of the lung showed "nodules consistent with an interstitial pneumonitis, with terminal bronchopneumonia."[7]

Another case, with similar post-mortem findings gave a history of recurrent bronchopneumonia. There was dullness with bronchovesicular breath sounds in both bases. In addition to reticulation, the x-ray film revealed bilateral basal opacities.

Illustrative Cases: 1) M.F., 6562F, white male, age 48, with advanced rheumatoid arthritis of two years duration. There were no pulmonary symptoms or physical findings. The x-ray film appearance was thought to be consistent with the above description (Fig. 7).

2) R.S., 12087F, white male, age 45, had had severe rheumatoid arthritis for 10 years. There was an occasional cough productive of a small amount of thick white sputum. There were scattered dry rales which cleared on coughing. A biopsied subcutaneous nodule was microscopically a typical rheumatic nodule. The pulmonary lesions seen in the x-ray film (Fig. 8) have not been examined histologically.

Erythema Nodosum: Erythema nodosum may give rise to no pulmonary symptoms, or to occasional cough. Physical findings are meager.

Roentgenologically there are enlarged hilar nodes, and occasionally slight pulmonary changes, such as might be called "acute bronchitis."[18] The appearance may be indistinguishable from sarcoidosis.[19] Distinction may be made on the basis of the skin lesions, however.

Dermatomyositis: Dermatomyositis is mentioned only because so many other "collagen diseases" have been discussed. No reports have been found of frequent or specific pulmonary lesions associated with it.[11,14,16,23]

SUMMARY

A number of non-infectious systemic diseases frequently include pulmonary lesions as a part of the picture. Among these, scleroderma presents the most characteristic and widely recognized findings, and rheumatoid arthritis the least frequently seen. Other diseases in this group with pulmonary manifestations include lupus erythematosus, rheumatic fever, periarteritis nodosa, and erythema nodosum. No pulmonary involvement is reported in dermatomyositis. Although the pulmonary lesions in these diseases are not sufficiently characteristic to lead to a diagnosis, they may give rise to suspicion; also, there may be confusion with other processes, such as tuberculosis and carcinoma.

RESUMEN

Cierto número de enfermedades generales no infecciosas frecuentemente presentan lesiones pulmonares como parte del cuadro clínico. De estas enfermedades, la escleroderma presenta los hallazgos más característicos y extensamente reconocidos y la artritis reumatoida los más raros. Otras enfermedades en este grupo con manifestaciones pulmonares incluyen el lupo eritematoso, la fiebre reumática, la periarteritis nodosa y el eritema nodoso. No se conoce ninguna afección pulmonar en la dermatomiositis. Aunque las lesiones pulmonares en estas enfermedades no son lo suficiente características para que se haga el diagnóstico, sí pueden causar sospecha. Además, es posible que causen confusión con otros procesos, tales como la tuberculosis y el carcinoma.

RESUME

Dans le tableau d'un certain nombre de maladies systématisées non infectieuses, on peut noter des lésions pulmonaires. La sclérodermie en comporte les éléments les plus caractéristiques et les plus largement reconnus, tandis que dans le rheumatisme articulaire, ils sont le moins fréquents. Cette catégorie de manifestations pulmonaires appartient à d'autres affections telles que le lupus érythémateux, la fièvre rhuùatismale, la périartérite noueuse et l'érythème noueux. Il n'y a pas de localisation pulmonaire connu dans les dermatomyosites. Bien que, dans ces affections, les manifestations pulmonaires ne soient pas suffisamment caractéristiques pour permettre d'en porter le diagnostic, elles permettent parfois de le suspecter. Elles peuvent être cependant l'occasion de confusions avec d'autres affections telles que tuberculose et cancer.

REFERENCES

1 Ayvasian, L. F. and Badger, T. L.: "Disseminated Lupus Erythematosus Occurring Among Student Nurses," *New Eng. J. Med.*, 239:565, 1948.

2 Bounet, W. L.: "Roentgen Findings in Erythema Nodosum," *Radiology*, 47:175, 1946.

3 Boyd, L. J.: "Pulmonary Manifestations of Periarteritis Nodosa," *Bull. New York M. Coll.*, Flower and Fifth Ave. Hosps., 7:94, 1944.

4 Cecil, R. L.: "A Textbook of Medicine," *W. B. Saunders Co.*, Phila., 1948.

5 Dostrowsky, A.: "Progressive Scleroderma of the Skin with Cystic Sclerodermal Changes of the Lungs," *Arch. Dermat. and Syph.*, 55:1, 1947.

6 Elkeles, A.: "Serial Roentgenograms of the Chest in Periarteritis Nodosa as an Aid to Diagnosis," *Brit. J. of Radiology*, 17:368, 1944.

7 Ellman, P. and Ball, R. E.: " 'Rheumatoid Disease' with Joint and Pulmonary Manifestations," *Brit. M. Jour.*, 2:816, 1948.

8 Epstein, E. Z. and Greenspan, E. B.: "Rheumatic Pneumonia," *Arch. Int. Med.*, 68:1074, 1941.

9 Getzowa, S.: "Cystic and Compact Pulmonary Sclerosis in Progressive Scleroderma," *Arch. Path.*, 40:99, 1945.

10 Gouley, B. A. and Eisman, J.: "The Pathology of Rheumatic Pneumonia," *Am. J. Med. Sc.*, 183:359, 1932.

11 Jager, B. V. and Grossman, L. A.: "Dermatomyositis," *Arch. Int. Med.*, 73:271, 1944.
12 Leys, D. G. and Swift, P. N.: "Pulmonary Lesions in Rheumatoid Arthritis," *Brit. M. Jour.*, 1:434, 1949.
13 Longcope, W. T.: "Scleroderma," *Oxford Medicine*, 6:828 (8), Oxford University Press, New York, 1945.
14 Marcus, A. H. and Weinstein, J.: "Dermatomyositis: Report of a Case," *Ann. Int. Med.*, 9:406, 1935.
15 Miller, H. G. and Daley, R.: "Clinical Aspects of Periarteritis Nodosa," *Quarterly J. of Med.*, 15:255, 1946.
16 O'Leary, P. A.: "Dermatomyositis," *M. Clin. N. Am.*, 33:21, 1949.
17 Rigler, L. G.: "The Chest," *A Handbook of Roentgen Diagnosis*, The Year Book Publishers, Chicago, 1946.
18 Rich, A. R. and Gregory, J. E.: "On the Anaphylactic Nature of Rheumatic Pneumonitis," *Bull. Johns Hopkins Hosp.*, 73:465, 1943.
19 Rothman, S. and Felsher, Z.: "Subacute and Acute Disseminated Lupus Erythematodes," *M. Clin. North Am.*, 31:198, 1947.
20 Sosman, M. C., Bailey, O. T. and Armstrong, H. S. Jr.: "Four Rare Diseases," Unpublished paper read before the American Roentgen Ray Society and the Radiological Society, Chicago, Sept. 26, 1944.
21 Swanberg, T.: "Roentgenological Pulmonary Changes in Periarteritis Nodosa," *Acta radiologica*, 26:307, 1945.
22 Sweeney, A. R. Jr. and Baggenstoss, A. H.: "Pulmonary Lesions of Periarteritis Nodosa," *Proc. Staff Meet., Mayo Clinic*, 24:35, 1949.
23 Turner, J. C.: "Dermatomyositis," *New Eng. J. Med.*, 126:158, 1937.
24 Weiss, S., Stead, E. A. Jr., Warren, J. V. and Bailey, O. T.: "Scleroderma Heart Disease with a Consideration of Certain Other Visceral Manifestations of Scleroderma," *Arch. Int. Med.*, 71:749, 1943.
25 Wigley, J. E. M., Edmunds, V. and Bradley, R.: "Pulmonary Fibrosis in Scleroderma," *Brit. J. Derm. and Syph.*, 61:324, 1949.

*Report of the Joint Committee on Chest X-Ray**

Committee of the American College of Radiology:

Leo G. Rigler, M.D., Minneapolis, Minnesota, *Chairman*
Sydney J. Hawley, M.D., Seattle, Washington
Russell H. Morgan, M.D., Baltimore, Maryland
E. P. Pendergrass, M.D., Philadelphia, Pennsylvania
Paul C. Swenson, M.D., Philadelphia, Pennsylvania

Committee of the American College of Chest Physicians:

Otto L. Bettag, M.D., Chicago, Illinois, *Chairman*
Robert J. Anderson, M.D., Washington, D. C.
Hollis E. Johnson, M.D., Nashville, Tennessee
Edward Kupka, M.D., Berkeley, California
James H. Stygall, M.D., Indianapolis, Indiana

PURPOSE OF JOINT COMMITTEE ON CHEST X-RAY

The purpose in having a Joint Committee on Chest X-ray is that two professional organizations, who have common interests, may exchange ideas and formulate unified thinking on the problems involved in routine chest x-rays in hospitals (general, mental, etc.), and mass chest x-ray programs. In addition to this the Committee, after considerable discussion, agreed to another point, namely: that each physician should be encouraged to have a chest x-ray on all of his patients.

LIMITS OF SURVEY

For purposes of this discussion routine chest survey examinations should be defined as those examinations of the chest which are conducted on microfilm apparatus for screening normal persons from those patients with abnormal changes in the chest. The examinations are screening and are not to be considered as diagnostic procedures. Screening method is for the purpose of detecting the presence or absence of a lesion but should not be utilized for identifying the nature of the pathological process.

The 14 x 17 inch film is fundamentally a diagnostic tool and its use, therefore, makes the examination more than a screening procedure. Survey chest x-rays, either in hospitals or in general population, are approved as a screening device if conducted by agencies which utilize well qualified professional technical staffs and which make a sincere effort to send the positive individuals to qualified local physicians or clinics for proper follow-up. The methods of conducting these were discussed at length. These included surveys by the U. S. Public Health Service, etc. Dr. Newell reported on the San Francisco County Medical Society's plan, whereby the medical society is responsible for the surveys but the project is financed through the local tuberculosis association.

*This report was prepared at a meeting of the joint committee held in San Francisco, June 26, 1950. On December 4, 1950, the report was approved by the Board of Regents of the American College of Chest Physicians, meeting in Cleveland, Ohio, and on February 7, 1951, by the Board of Chancellors of the American College of Radiology, meeting in Chicago, Illinois.

INTERPRETATION AND REPORT

Interpretation and reporting of medical findings is a medical matter and should bear the signature or identification of the responsible physician.

METHOD OF REPORTING

Method of reporting of chest survey studies: This is a local matter and is by prearranged agreement between the employer and the employee in industrial surveys; in other surveys is in accord with medical ethics, according to local agreement.

TYPE OF REPORTING

Type of reporting: The Committee discourages the reporting of suspicious cases as tuberculosis. It believes this to be a clinical diagnosis. The x-ray interpreter should designate the cases that require immediate follow-up as "urgent." The small film x-ray interpretation is merely an impression.

It should be emphasized that the 14 x 17 inch film is a diagnostic aid and the results derived therefrom are also impressions and not diagnoses. Even the larger film is but one of several examinations necessary in order to establish correct diagnoses.

PROFESSIONAL COMPENSATION

The professional cost of performing routine chest examinations in hospitals: The Joint Committee believes the radiologist and/or chest physician should be compensated just as any other physician practicing his profession. The procedure is time consuming and places a definite responsibility on the radiologist or chest physician. The Committee likewise felt that in this matter the basic principle of payment is by arrangement between the physician and the hospital or agency involved. In the reading of follow-up films there should also be an individual limit to the number of films which should be read in any one day by one physician and which he should not exceed. The compensation, of course, would have to take into consideration whether the physician not only reads the film but also makes the film.

CLOTHING OF PATIENTS

Whether or not a screening examination can be conducted with the patient fully clothed: Since the number of lesions overlooked because of clothing (2 per cent) is considerably smaller than the normal variations of interpretation Chamberlin, etc., have demonstrated to exist in the reading of photofluorographic films, it was concluded that the examination of clothed persons was as effective a procedure as examination of the undressed persons. Since examination of the fully clothed persons is an easier procedure as compared with the examination of the undressed persons, the Committee agreed that screening examination can be conducted with the patient fully clothed.

READERS' QUALIFICATIONS

Qualifications of readers in mass chest surveys: It was believed at the present time there was no practical method which could be used to evaluate the qualifications of a particular reader. Studies in this respect

are being made at the present time. It is hoped that within a short period of time satisfactory testing methods will be available. The Committee therefore agreed to leave this matter open for further discussion.

CONCLUSION

The two Committees agreed that the bi-committee arrangement should continue and that another meeting be arranged in at least one year. In an effort to have the committees act continuously and without interruption, interim ideas should be sent to the respective chairmen and an exchange of opinions should continue during the meeting interval.

The Oxford Conference

The Oxford Conference on Tuberculosis and Diseases of the Chest will be held at Oxford, England, July 16 through 21, 1951, sponsored by the Faculty of Radiologists, Society of Thoracic Surgeons, Tuberculosis Society of Scotland, Society of Medical Officers of Health, British Paediatric Association and the British Tuberculosis Association. Participants in the Conference will assemble on Monday evening, July 16. The next three days, July 17, 18 and 19, will be devoted to lectures and discussions. On Friday, July 20, the Conference will disperse to various thoracic centers throughout the country where members will have the opportunity to see operations, demonstration of techniques, etc. Further particulars may be obtained from the Hon. Sec. Dr. Stephen Hall, 16 Grosvenor Place, London, S.1.W., England.

The program of speakers and subjects for July 17, 18 and 19 are as follows:

"Tuberculin Surveys,"
Marc Daniels (Medical Research Council Research Staff'),
Margaret Macpherson (Brompton Hospital).

"Vaccination with the Vole Bacillus,"
A. Q. Wells (Oxford), J. Young (Cambridge).

"Treatment of Tuberculous Meningitis,"
Honor Smith (Oxford), R. S. Illingworth (Sheffield).

"Present Position of Chemotherapy in Tuberculosis,"
J. W. Crofton (Brompton Hospital), L. E. Houghton (Harefield Hospital), Christopher Clayson (Lochmaben Sanatorium).

"Bronchiectasis in Children,"
A. L. d' Abreu (Birmingham), J. H. Hutchison (Glasgow).

"Rehabilitation and Resettlement,"
J. E. Geddes (Birmingham).

"Cardiac Surgery,"
R. C. Brock (Brompton Hospital), Price Thomas (Brompton Hospital), Oswald Tubbs (Brompton Hospital), Holmes Sellors (London Chest Hospital).

"Pneumoconiosis,"
C. M. Fletcher (Pneumoconiosis Research Unit).

"Pulmonary Resection for Tuberculosis,"
F. H. Young (Brompton Hospital), Ronald Edwards (Liverpool), V. C. Thompson (London Chest Hospital).

SEVENTEENTH ANNUAL MEETING OF THE COLLEGE

Ambassador Hotel, Atlantic City, New Jersey

JUNE 7 THROUGH 10, 1951

One Hundredth Annual Session
AMERICAN MEDICAL ASSOCIATION
Atlantic City, June 11 - 15, 1951

Advance reservations for the annual meeting of the College to be held in Atlantic City, June 7 through 10, have been made in great number. The Ambassador Hotel, headquarters for the College meeting, has reported that accommodations are still available, but that the number of remaining rooms is limited. Members are urged to make their reservations at once by writing directly to the Ambassador Hotel, Atlantic City.

Dr. Edwin R. Levine, chairman of the Committee on Scientific Program for the College meeting, has announced that the program is almost completed.

A feature of the program will be symposiums on subjects whose scope is so broad that discussions, rather than presentation of papers, would appear to be more valuable. The committee has selected as panel members research and clinical workers who can discuss the various subjects out of their own personal experience. It is hoped that the audience will ask questions and also make comments so that the session will be a generalized discussion led by people with specialized knowledge and experience. These symposiums are scheduled as follows:

FRIDAY, JUNE 8, 3:00 to 5:00 p. m.:

ACTH and Cortisone in Diseases of the Chest,
Edwin R. Levine, Chicago, Illinois, Moderator.

Panel: Emil Bogen, Olive View, California, Tuberculosis.
James M. Carlisle, Rahway, New Jersey, Cortisone.
Irene Ferrer, New York, New York, Cardiac and pulmonary conditions.
Maurice S. Segal, Boston, Massachusetts, Asthma and other chest conditions.
Randall G. Sprague, Rochester, Minnesota, Emphysema.

SUNDAY, JUNE 10, 10:00 to 12:00 noon:

Chemotherapy and Antibiotics in Diseases of the Chest,
Karl H. Pfuetze, Chicago, Illinois, Moderator.

Panel: Carl W. Tempel, Denver, Colorado, Tuberculosis.
Alvan L. Barach, New York, N. Y., Asthma and emphysema.
Sumner S. Cohen, Oak Terrace, Minnesota, Tibione and other chemotherapeutic agents.
Gladys L. Hobby, Brooklyn, N. Y., Viomycin.
Alvis E. Greer, Houston, Texas, Fungus diseases, pneumonias, etc.
Eugene T. McEnery, Chicago, Illinois, Diseases of the chest in children.

SUNDAY, JUNE 10, 3:00 to 5:00 p. m.:

Occupational Diseases of the Chest,

This symposium is presented jointly by the American Association of Industrial Physicians and Surgeons and the American College of Chest Physicians.

Edward C. Holmblad, Chicago, Illinois, Moderator.

Panel: O. A. Sander, Milwaukee, Wisconsin, Classification of dust and siderosis.
L. E. Hamlin, Chicago, Illinois, Silicosis.
Louis L. Friedman, Birmingham, Alabama, Anthracosilicosis.
Frank Princi, Cincinnati, Ohio, Treatment and rehabilitation.
George R. Meneely, Nashville, Tennessee, Pulmonary function tests.

Other members of the panel will include: Burgess Gordon, Philadelphia; J. Gough, Cardiff, Wales, Great Britain; Edgar Mayer, New York City; Leo G. Rigler, Minneapolis; Reginald Smart, Los Angeles; Arthur J. Vorwald, Saranac Lake; and C. Richard Walmer, Pittsburgh.

Regular features which have been popular in past years and which will be repeated this year include:

X-Ray Conference, Saturday, June 9, 2:00 to 4:30 p. m.
Conducted by Leo G. Rigler, Minneapolis, Minnesota.

Motion Picture Session, Friday, June 8, 8:00 p. m.
Paul H. Holinger, Chicago, Illinois, Chairman.

Another interesting evening of medical motion pictures is being prepared by Dr. Paul H. Holinger consisting of films not previously shown at these meetings.

Six luncheon round table discussions will be held on each of the three days of the meeting, Friday, Saturday and Sunday, June 8, 9 and 10. These are under the direction of Harold G. Trimble, Oakland, California. The subjects and moderators will be announced in a future issue of *Diseases of the Chest*.

Papers to be presented in the regular scientific sessions of the annual meeting are as follows:

Exploratory Surgery of the Heart,
Charles P. Bailey, Philadelphia, Pennsylvania.

Venous Pressure as a Guide to Pneumoperitoneum Therapy in Pulmonary Emphysema,
Gustav J. Beck and Chesmore Eastlake, New York, New York.

Title to be announced,
Ignacio Chavez, Mexico City, Mexico.

Bronchiectasis in Children,
Lloyd B. Dickey, San Francisco, California.

Relation of X-ray Survey to Bronchogenic Carcinoma (Committee Report),
Alfred Goldman, Beverly Hills, California, Chairman.

Studies in Pericarditis,
George R. Herrmann, Galveston, Texas.

The Status of Tried Procedures in the Treatment of Pulmonary Tuberculosis as Seen in the Light of Thirty Years Experience,
William A. Hudson and Willard B. Howes, Detroit, Michigan.

The Relationship Between Pathological Changes in Blood Vessels in Resected Lobes and Lungs as Correlated with Pulmonary Artery Pressure Changes Recorded During Cardiac Catheterization,
Allan Hurst, Denver, Colorado.

Recovery of Pulmonary Function After Crushing Injuries of the Chest,
N. K. Jensen, Minneapolis, Minnesota.

A Study of Delayed Non-Specific Tuberculin Reactions,
M. R. Lichtenstein and Carmine Cilella, Chicago, Illinois.

Physiologic Factors in the Use of the Respirator for Impairment of Respiratory Function,
J. V. Maloney, Jr., Baltimore, Maryland.

The Effect of the Diminishing Incidence of Primary Infection on the Tuberculosis Control Program,
Jay Arthur Myers, Minneapolis, Minnesota.

Respiratory Air Flow and Related Measurements in Pulmonary Disease,
Donald F. Proctor, Baltimore, Maryland.

The Application of Pancreatic Enzyme in the Treatment of Tuberculous Empyema,
Louis C. Roettig and Louis Mark, Columbus, Ohio.

Relationship of the Autonomic Nervous System and Peripheral Vascular Bed to the Acute Pulmonary Edema State,
Stanley J. Sarnoff, Boston, Massachusetts.

Clinical Diagnosis of Pseudo-Truncus Arteriosus,
Helen B. Taussig, Baltimore, Maryland.

Follow-up of Pneumothorax (Committee Report),
Harold G. Trimble, Oakland, California, Chairman.

The Recognition of Non-allergic Asthma,
Leon Unger, Chicago, Illinois.

Current Concepts on the Etiology of the Common Cold,
Thomas G. Ward, Baltimore, Maryland.

Pectus Excavatum,
Francis M. Woods, Richard H. Overholt and H. E. Bolton, Boston, Massachusetts.

SAN FRANCISCO POSTGRADUATE COURSE

The postgraduate course in diseases of the chest sponsored by the American College of Chest Physicians, California Chapter, in cooperation with the University of California and Stanford University Schools of Medicine was presented at the University Extension Building in San Francisco during the week of February 19 through 23. The course was attended by 36 physicians representing several Western States and Canada. A dinner sponsored by the California Chapter of the College and the Laennec Society was held on Monday evening, February 19, which was attended by approximately 125 physicians. Dr. Alvan L. Barach, New York City, and Dr. Burgess Gordon, Philadelphia, were guest speakers. Dr. Stacy R. Mettier, Head of Postgraduate Instruction, Medical Extension, University of California Medical Center, San Francisco, spoke briefly at the banquet.

College Chapter News

FLORIDA CHAPTER

An informal meeting of the members of the Florida Chapter of the College was held on March 9 at the winter residence of Dr. George G. Ornstein in Fort Lauderdale. Dr. Louis Mark, Columbus, Ohio, President of the College and Dr. Burgess Gordon, Philadelphia, Governor of the College for Pennsylvania were present to participate in the scientific session which followed a buffet dinner.

Alexander Libow, *Secretary*.
Nathaniel M. Levin, *Chairman, Program Committee*.

GEORGIA CHAPTER

A meeting of the Georgia Chapter of the College was held in Atlanta on February 27. The meeting opened with a dinner at the Atlanta Biltmore Hotel which was presided over by Dr. Carl C. Aven, Governor of the College for Georgia. Mr. Murray Kornfeld, Executive Secretary of the College, met with the members and their guests at this meeting. An evening scientific session was presented at the Academy of Medicine in which the following papers were presented:

"Atypical Pulmonary Lesions with Special Reference to Loeffler's Syndrome,"
Louis Mark, Columbus, Ohio.

"Clinical and Physiological Management of Chronic Pulmonary Diseases,"
Burgess L. Gordon, Philadelphia, Pennsylvania.

"Anthracosilicosis,"
Louis L. Friedman, Birmingham, Alabama.

At the business session of the chapter, the following officers were elected for the coming year:

A. Worth Hobby, Atlanta, President
J. C. Burch, Atlanta, Vice-President
Joseph S. Cruise, Atlanta, Secretary-Treasurer

Dr. William A. Hopkins of Atlanta was appointed chairman of the program committee for the Georgia Chapter.

Joseph S. Cruise, *Secretary*.

PERUVIAN CHAPTER

At a recent meeting of the Peruvian Chapter of the College the following officers were elected for the ensuing year:

Juan Escudero Villar, Lima, President
Leopoldo Molinari Balbuena, Lima, Vice-President
Angel Luis Morales, Lima, Secretary
Luis E. Hübner, Callao, Treasurer
Alejandro Flores Degregori, Lima, Librarian

ILLINOIS CHAPTER

The annual meeting of the Illinois Chapter will be held at the Sherman Hotel, Chicago, on Wednesday, May 23, in conjunction with the meeting of the Illinois State Medical Society. The scientific session will be presented at 9:30 a. m. consisting of the following papers:

"Recent Advances in the Treatment of Bronchial Asthma with Special Reference to the Use of ACTH and Cortisone,"
Maurice S. Segal, Boston, Massachusetts.

"Some of the Problems in the Diagnosis of Congenital Malformations of the Heart,"
Benjamin M. Gasul, Chicago, Illinois.

"The Treatment of Bilateral Bronchiectasis,"
Darrell H. Trumpe, Springfield, Illinois.

"Immunological Considerations in Tuberculosis, with Special Reference to Vaccination,"
Jay Arthur Myers, Minneapolis, Minnesota.

"The Use of the Chest X-Ray in Picking up a Masquerading Lung and Heart Condition,"
Abel Froman, Chicago, Illinois.

The scientific session will be followed by the annual luncheon and business meeting.

On March 16 the Illinois Chapter held a joint meeting with the Chicago Tuberculosis Society at the Congress Hotel, Chicago. The following subjects were presented:

"The Effect of Cortisone on Tuberculosis in the Guinea Pig,"
Robert G. Bloch, Chicago, Illinois.

"The Use of Pulmonary Biopsy in Diffuse Pulmonary Lesions,"
Karl P. Klassen, Columbus, Ohio.

"The Clinical Applications of Radioactive Isotopes and Their Use in the Diagnosis of Chest Tumors,"
Morris T. Friedell, Chicago, Illinois.

William J. Bryan, *Secretary*.
Abel Froman, *Chairman, Program Committee*.

ROCKY MOUNTAIN CHAPTER

The Rocky Mountain Chapter of the College held an x-ray clinical symposium at the Shirley-Savoy Hotel, Denver, March 17. The meeting opened with a luncheon at 1:00 p. m. attended by chapter members and guests.

W. Bernard Yegge, *Secretary*.
Fred R. Harper, *Chairman, Program Committee*.

URUGUAY CHAPTER

The Uruguay Chapter of the College met in annual session on September 29, 1950, at Montevideo, at which time the following officers of the chapter were elected:

Felix E. Leborgne, President
Raul A. Piaggio Blanco, Vice-President
Alejandro C. Artagaveytia, Secretary-Treasurer

POTOMAC CHAPTER

The Potomac Chapter of the College will meet at 2:00 p. m. on Thursday, May 24, at the District of Columbia Medical Society Building, Washington, D. C. The program is as follows:

Symposium on the Unexpanded Lung:

"Introduction,"
Hugh G. Whitehead, Baltimore, Maryland,
President, Potomac Chapter.

"Medical Aspects,"
Dean B. Cole, Richmond, Virginia.

"Surgical Aspects,"
Otto C. Brantigan, Baltimore, Maryland.

"Surgical Aspects,"
Edgar Davis, Washington, D. C.

"Physiological Aspects,"
Richard Riley, Baltimore, Maryland.

General Discussion.

The scientific session will be followed by a cocktail party and dinner to be held at the Mayflower Hotel.

Milton B. Kress, *Secretary.*

PHILIPPINE CHAPTER

The Philippine Chapter of the College, in cooperation with the Quezon Institute, presented a postgraduate course in diseases of the chest during the week of February 5 through 10. The course was presented at the Quezon Institute Social Hall, Manila, and was arranged under the direction of Dr. Miguel Canizares, Regent of the College for the Philippine Islands. Dr. Fidel R. Nepomuceno, Secretary-Treasurer of the Philippine Chapter of the College, served as Secretary and Registrar for the postgraduate course. The chapter plans to organize similar courses in the future.

COURSE IN BRONCHOESOPHAGOLOGY

The next course in bronchoesophagology will be given May 21st to June 1st, 1951. For application forms and further information please communicate with the Department of Bronchoesophagology, Laboratory 604, Temple University School of Medicine, 3400 North Broad Street, Philadelphia 40, Pennsylvania.

Chevalier Jackson and Chevalier L. Jackson.

AMERICAN COLLEGE OF PHYSICIANS

A series of postgraduate courses pertaining to various phases of internal medicine have been scheduled for the spring of 1951 by the American College of Physicians. Programs and application forms may be obtained by writing to the executive secretary, Mr. E. R. Loveland, at 4200 Pine Street, Philadelphia 4, Pennsylvania.

College News Notes

A meeting of the joint committee on occupational diseases of the chest representing the American Association of Industrial Physicians and Surgeons and the American College of Chest Physicians was held at the Atlanta Biltmore Hotel, Atlanta, Georgia, on Tuesday afternoon, February 27. Those present were Dr. Louis L. Friedman, Birmingham, Alabama; Dr. Burgess Gordon, Philadelphia, Pennsylvania; Dr. L. E. Hamlin, Chicago, Illinois; Dr. Edward C. Holmblad, Chicago, Illinois; Dr. Louis Mark, Columbus, Ohio; Dr. George R. Meneely, Nashville, Tennessee; Dr. Frank Princi, Cincinnati, Ohio; Dr. O. A. Sander, Milwaukee, Wisconsin; Dr. C. Richard Walmer, Pittsburgh, Pennsylvania; and Mr. Murray Kornfeld, Chicago, Illinois, Executive Secretary of the College. At this meeting plans were discussed for a symposium on occupational diseases of the chest to be presented at the annual meeting of the College in Atlantic City in June.



Dr. Moses J. Stone, Boston, addressed members of the Israeli Chapter of the College on October 11, 1950. His subject was "Recent Trends in the Treatment of Pulmonary Tuberculosis." The above photograph was taken of Dr. Stone and some of the officers and members of the Israeli Chapter.

Dr. Aleksei A. Leonidoff, president of the medical staff of St. Francis Hospital, Poughkeepsie, New York, was honored at a testimonial dinner on February 1. The testimonial was arranged in recognition of his completion of 35 years of medical service.

Dr. Richard P. Jahn and Dr. Joseph Kuzma spoke before the Milwaukee Metropolitan Section of the College at the Medford Hotel, Milwaukee, Wisconsin, on Friday, February 23. Their subject was "Egg Shell Calcification."

Dr. Walter E. Vest, Huntington, West Virginia, was named president elect of the Federation of State Medical Boards of the United States at the annual meeting in Chicago, February 13, 1951. Dr. Vest is chairman of the medical licensing board of West Virginia and for many years was president of the public health council prior to the creation of the new licensing board.

Dr. John S. Bouslog, Denver, Colorado, took office as president of the Radiological Society of North America at their annual meeting held in Chicago, December 10-15, 1950.

Dr. Allan Hurst, medical director of the National Jewish Hospital, Denver, has just returned from a four-week survey of the tuberculosis problems in Israel, where he went at the invitation of the Kupat-Holim (Workers' Sick Fund). During his stay there he delivered a lecture at the tuberculosis hospital at Ranaana before the entire Tuberculosis Organization of Israel on "The Use of Plastic Substances in Extrapleural Plombage." He also lectured on "The Present Status of Cardio-pulmonary Function Studies" at the Hadassah Medical School in Jerusalem, the Haifa Medical Association, and the Beilinson Hospital in Petach Tikva. Additional lectures were given on the "Social and Emotional Aspects of Tuberculosis" in Jerusalem, and "The Place of Occupational Therapy in the Rehabilitation of the Tuberculous." Dr. Hurst is preparing a report of his findings in Israel for the Kupat-Holim and the government.

Dr. Jacob J. Mendelsohn, Chicago, Illinois, addressed the Milwaukee Metropolitan Section of the College on Friday, January 26 at a dinner meeting at the Medford Hotel in Milwaukee. His subject was "The Maurer Method of Cavity Exteriorization and Tamponade" which was illustrated with a moving picture and followed by a round table discussion. Dr. Mendelsohn presented the same subject at a meeting of the Florida Chapter of the College held at the Veterans Hospital in Miami on Feb. 9.

Dr. John F. Briggs, St. Paul spoke on the subject of cardiac arrhythmias at a meeting of the Minnesota Society of Anesthesiologists in St. Paul on December 2.

Dr. Chevalier L. Jackson, Philadelphia, Pennsylvania, presented the subject of "Treatment of Esophageal Disease" at the Annual Clinical Conference of the Chicago Medical Society held on March 6-9.

Dr. Andrew L. Banyai, Milwaukee, Wisconsin, will speak at the annual session of the Missouri State Medical Association in Kansas City, April 22-25. His subjects will be "Modern Treatment of Cough" and "The Caprices of Sarcoidosis."

Dr. Benjamin M. Gasul, Chicago, Illinois, was appointed research associate at the annual meeting of the Board of Trustees of the Hektoen Institute for Medical Research.

An Institute of Cancer Cytology was recently chartered with headquarters in New York City. Dr. Seymour M. Farber, San Francisco, California, has been elected a member of the board of directors of the new institute.

Dr. Hilbert Mark, director of the Division of Tuberculosis Control of the Minnesota Department of Health since 1937, left on January 1 to assume directorship of tuberculosis control for the city and county of Denver, Colorado. In Denver he will head a tuberculosis clinic, a section of the general hospital, and a part of the University of Denver Medical School.

Book Review

The Management of the Patient with Severe Bronchial Asthma. By Maurice S. Segal, M.D., Assistant Professor in Medicine, Tufts College Medical School, Boston, Massachusetts. Charles C. Thomas Publisher, Springfield, Illinois, American Lecture Series, 1950, 176 pages, 16 illustrations, 7 tables.

There is probably no problem quite as discouraging to the practitioner of medicine as the patient with severe intractable asthma. Acute attacks of asthma that respond to adrenalin or some other such one-time treatment are not so bad. Both the patient and the doctor feel that a disease condition has been met and successfully treated. But the severe asthma continuing hour after hour and day after day, despite injections and medications, discourages the doctor, the patient and the patient's family. If this were a rare condition we would put it down as one of those unfortunate episodes in medicine that we hope not to encounter too frequently, but asthma of this type is encountered only too often by the specialist in diseases of the chest and so becomes a problem, difficult as it may be, that he must be prepared to face at any time.

Under such circumstances the appearance of this book by Dr. Segal is a very welcome event. In the space of very few pages, with an admirable conciseness, he has discussed the pathological physiology and therapy of this condition from the standpoint of allergy, of bronchial mechanisms, the use of drugs, and the management of complications.

It is perfectly obvious that the variability of the asthmatic state is such, in relation to the differences in patients, previous pathology, and etiology, so that no single method of treatment will be effective in all cases. Despite the hopes that were raised with the introduction of aminophyllin, antihistamines, and most recently, ACTH and cortisone, a perusal of this volume indicates that these and other agents which have yet to be discovered, must be used as part of a physiologic approach to what is a physiologic derangement. It emphasizes the understanding of therapy and the principles which underlie any particular method, rather than a simple description of the treatment of isolated cases. It can and should be used as general reading matter to furnish a background in asthma, as a reference for the use of any particular method, and to provide a basis on which the use of future therapeutic agents may be determined.

Edwin R. Levine.

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COLLEGE EVENTS

17th Annual Meeting, American College of Chest Physicians, Atlantic City, New Jersey, June 7-10, 1951.

Milwaukee Postgraduate Course for General Practitioners, Apr., 1951
Missouri Chapter Meeting, Kansas City, April 22, 1951.
Virginia Chapter Meeting, Richmond, April 25, 1951.
Minnesota Chapter Meeting, Rochester, April 30, 1951.
Texas Chapter Meeting, Galveston, April 30, 1951.
New York State Chapter Meeting, Buffalo, May 3, 1951.
California Chapter Meeting, Los Angeles, May 12, 1951.
Illinois Chapter Meeting, Chicago, May 23, 1951.
Potomac Chapter Meeting, Washington, D. C., May 24, 1951.
Chicago Postgraduate Course, September 24-28, 1951.
Minneapolis Postgraduate Course, October 18-20, 1951.
New York City Postgraduate Course, November 12-17, 1951.

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People who develop "prolonged" diseases—diabetes, structural heart disease, rheumatic fever, tuberculosis and similar chronic disorders—need to be emotionally prepared for the months or even years of altered living ahead of them, according to Dr. George Saslow of Washington University, St. Louis. In the December issue of GP, journal of the American Academy of General Practice, published today, Dr. Saslow points out that not only do these patients have a better mental outlook, if they can become psychologically adjusted to the limitations of their disease—their chances of improvement and ultimate cure are greatly increased.

He points to diabetic and tuberculus patients as notoriously prone to become discouraged and indifferent regarding their doctors' instructions. "Thirty to seventy per cent of hospitalized tuberculus patients do not complete their treatment; no matter how good the hospital, they leave without permission. A fair number of these people are dead within a year, having spread infection to an unknown number of persons in the meantime.

"It appears that, unless the patient with chronic illness is helped to achieve the necessary level of sustained cooperation, we shall often fail to give him the benefit of our best medical and surgical knowledge. Threats of certain disability or death are less effective than we would like to believe."

Recognizing that a person acquiring a chronic disease has a right to know exactly what is wrong with him, and that the news is going to be emotionally disturbing, Dr. Saslow observes that the patient will not be able "to look at his total predicament objectively if he is simply preached at, or if the situation's difficulty is minimized."

First of all, the patient needs to be allowed to release his emotions — to "get it out of his system" — by expressing his distress and fears. It is

almost inevitable for most patients to be emotionally distressed by news of their condition, according to the author, particularly if it had not been previously suspected. This distress is expressed in many different forms: "Some patients show apparent apathy; others appear stunned; some cry, insist the physician is wrong, or become angry at some person believed to be the source of infection. Others fear loss of friends or promising careers, are overwhelmed by the realization of their prospective dependency or of the economic implications."

The GP article suggests, however, that if the patient is given an opportunity to bring these fears and tensions out into the open, and that if the physician will then calmly and thoroughly discuss the condition and probable outlook for the future, the patient will in most instances be able to adjust himself to the new situation. In doing this he acquires not only the courage to face the future, but also an understanding of the cooperation he must be prepared to give the physician, hospital attendants, and members of his family, if he is to make the best possible recovery.

Physical signs may be absent with early activity or with indolent or deep-seated tuberculous lesions. Tumors, cysts, and deep-seated abscesses may give no significant physical signs. Roentgen examination usually discloses more extensive disease than has been expected from other methods of examination. It is the only method by which the diagnosis of miliary tuberculosis can be made, since these tiny parenchymal lesions produce no distinctive clinical signs.

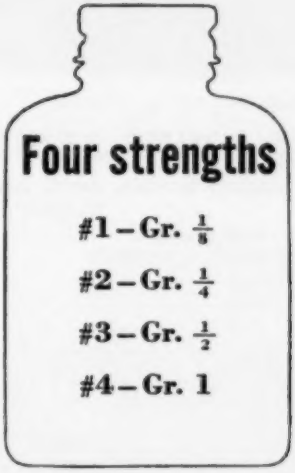
Sputum tests, a positive tuberculin test, gastric washings, and serial X-rays studies will usually establish or exclude the diagnosis. One should never make the diagnosis from roentgenologic findings alone, no matter how "typical" the shadows appear.—Am. Acad. General Prac., F. Kenneth Albrecht, M.D., April, 1950.

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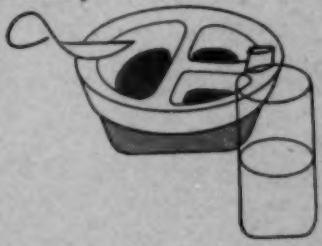


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Ref. 1. Meyer and Ragan: Science — 108, (Sept. 10th, 1948).
2. Schaeffer, Rashkoff & Magibow: Circulation, 265, (August 1950).
3. Gorsuch: Medical Woman's Journal, 57:9, (Sept. 1950).
4. Meyer and Ragan: Modern Concepts of Cardiovascular Disease *XVII*:No. 2 (Feb. 1948).
5. Camelin, Steiger & Tary: Presse Med. 58: 889, (Aug. 12th, 1950).
6. Ory: Brussels-Med. 29, 1401 (June 26, 1949).

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